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POLYNEURITIS GRAVIDARUM A "PRESUMABLE" TOXEMIA OF PREGNANCY

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WE RECOGNIZE a number of serious conditions which may complicate pregnancy, designated as the toxemias, including eclampsia and preeclamptic toxemia, nephritic toxemia, pernicious vomiting, and the like. While we still have to admit a profound ignorance in regard to the exact etiology of these conditions, they are universally regarded as being of a toxic origin, and all may present marked disturbances of general metabolism.

In addition to this more or less well defined group, there is still another group of cases which are much less frequently seen and even less well understood, which are usually classed as presumable toxemias. Under this category we may include certain psychoses, excessive salivation, the noncontagious skin lesion impetigo gestationis, a rare but highly fatal malady, and certain examples of multiple neuritis. This latter is a condition which is quite distinct from the more frequently seen traumatic and infectious types, and illustrating which we desire to present some of the findings noted in three patients whom we had the opportunity of observing recently.

Not infrequently women are seen who in the latter weeks of pregnancy complain of numbness and tingling in the hands and arms, with possibly more or less severe radiating pains in the shoulders and arms or possibly the lower extremities. These symptoms may give rise to considerable discomfort, but the general health is ordinarily not affected except possibly from loss of sleep. These patients may be regarded as suffering from a mild form of peripheral neuritis, of possibly toxic origin. Considerable relief may be given the patient by the application

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of heat and the employment of massage, while mild sedatives may occasionally be necessary to promote sleep. The symptoms ordinarily subside entirely in the puerperium.

At times a more severe type is observed in which the injury to one or more nerves is so extensive as to cause an actual paralysis of the muscles which they supply. This may occur during the course of pregnancy or may even originate during the puerperium. In this type, there is usually numbness and tingling in the affected parts, followed by pain, and this in turn succeeded by weakness and paralysis. There may be no disturbance of general health. The prognosis so far as life is concerned is usually good in this group, although the vagus and phrenic nerves might become involved in degenerative processes. After a rather prolonged convalescence, the paralysis may clear up entirely, though in some instances there may be a permanent residual disability, and atrophy of the affected muscles. One or more of the cranial nerves may be affected.

In a third group of patients a much more serious state of affairs is encountered. The patients appear profoundly ill. There is persistent vomiting with rapid and progressive loss of weight. There may be quite profound mental disturbances and progressive involvement of various nerves with paralysis of the corresponding muscles. The mortality in this group is high and is generally about 25 per cent.

Whether these three groups simply represent degrees of the same toxic process, or separate and distinct conditions it is impossible to say, as the toxic agent is unknown. Especially in the last group, there would seem to be little doubt as to the toxic nature of the condition, though in any given patient presenting the signs and symptoms of neuritis during pregnancy or the puerperium, it is necessary to exclude other possible causes of neuritis such as lead, alcohol, infections, etc., before regarding it as a toxemia of pregnancy.

While the condition has been recognized as a complication of pregnancy and the puerperium for a long time, it occurs very infrequently in the severe form and no one person has had the opportunity of observing a large series of cases.

Among the earliest references to the condition is a paper by Churchill, published in 1854, in which he reports a case of paralysis following delivery observed by himself, and collected 33 other examples of various types. Only a few of these apparently fall into the group caused by peripheral lesions of the nerves, many of the others being of the hemiplegic type. Churchill suspected the possibly toxic nature of the conditions on account of the association of albuminuria at times.

Möbius in 1887, reported seven cases of peripheral neuritis, all occurring in the puerperium, and with no associated general disturbances. None of these were due to trauma, and all recovered. He subsequently reported several other cases of a similar nature. Apparently, the earliest recorded case associated with severe vomiting and a profound general disturbance is that of Whitfield reported in 1889. He ascribed the neuritis, and the resulting paralysis to the persistent vomiting. This was undoubtedly one of the severe toxic type. The patient recovered. In the same

year Denos, Pinard, and Joffroy (quoted by Möbius) described a similar one. Lindemann, in a fatal case reported by Solowieff, found at autopsy in addition to lesions of various peripheral nerves, a fatty degeneration of the liver with cloudy swelling, and degenerative changes in the kidneys. Similar lesions were found in the liver and kidneys of the fetus. He did not regard these lesions as specific. During the illness of this patient, Solowieff recorded the interesting observation that the stomach contents contained no hydrochloric acid, this being ascribed at the time to the fact that she had been taking "soda water." This patient also presented marked mental disturbances during her illness.

Von Hösslin, in 1905, wrote an excellent review of the subject and collected 94 cases from the literature, including several observed by himself. The reader is referred to his article for a complete bibliography up to that time. His series included all types, in some only a single nerve being involved, in others groups of nerves, while still others were of the severe type with progressive general paralysis, and associated severe vomiting and mental disturbances. In those patients presenting a generalized paralysis, he found the mortality to be 20 per cent.

Von Hösslin did not feel that interruption of the pregnancy was necessarily indicated in this condition, even in the severe form. He based this statement on the fact that many patients improved without having the pregnancy interrupted, and also on the fact that termination of the pregnancy was not necessarily followed by improvement. Furthermore, in not a few patients, the first symptoms appear in the puerperium, several days or even more after the pregnancy has come to an end. In the presence of a vital indication, or developing blindness, however, he conceded that pregnancy should be interrupted.

Other observers, such as Schauta, Windscheid, and Johannsen felt that pregnancy should be interrupted in those instances where improvement failed to occur following palliative treatment.

Among the most recent series reported is that of Albeck, who presented 9 cases of the severe type with severe vomiting, psychoses, and progressive paralysis. In 7 of them pregnancy was interrupted, all apparently recovered, though the convalescence was prolonged, and months elapsed before normal muscular function was restored.

Seitz regards the disease as of toxic origin (other possible causes having been excluded). He believes that only in the severe cases is interruption of the pregnancy called for, and especially if the optic or phrenic nerves show signs of involvement. He also states that interruption of the pregnancy does not necessarily insure a good result, this conclusion being drawn from the fact that so many cases develop in the early puerperium. He cites a case of A. Meyer treated successfully during pregnancy by the injection of 10 c.c. of serum from a healthy pregnant woman.

Several instances of this condition associated with death of the ovum in utero are recorded. Madge, in 1871, recorded a case in which death of the ovum occurred at four months with retention of it for seven months longer before it was expelled spontaneously. This patient developed extensive paralysis of the peripheral type, but recovered completely before expulsion of the ovum.

Korsakow reported a case of paralysis resulting from peripheral neuritis, in which the child died several days before delivery. Death of the child did not bring about immediate improvement, the convalescence being long drawn out, and some permanent paralysis persisting. Korsakow and Serbski observed an example of the condition associated with advanced extrauterine pregnancy and dead fetus.

In none of the examples of this presumable toxemia reported up to the present time, has there been any attempt to study the changes which occur in the general metabolism of the patients affected. In the three

patients we recently observed, we had the opportunity to obtain a number of observations along this line which proved to be of considerable interest. The course of events in these patients may be briefly presented as follows:

CASE 1.—(Unit No. 18232) A nineteen-year-old primipara, admitted in September, 1928, when she was approximately four months pregnant, complaining of persistent vomiting for the past week. Examination revealed an obese white woman, weight 82 kilos, pulse 130, temperature 37° C., blood pressure 115/80, four months pregnant. The blood picture was normal, urinalysis negative, and general physical examination revealed no gross abnormalities. Wassermann negative. Routine chemical examination of the blood showed no unusual findings other than a CO_2 combining power of 71 per cent, the very upper limit of normal, a finding to which proper significance was not attached at the time. Mentally, her memory was defective, and at times she acted in a rather erratic manner. She did not create the impression of being seriously ill, and was placed on the usual treatment for persistent vomiting, being given infusions of glucose as well as normal saline. She responded well to this and was discharged after eight days. Readmitted October 28, 1928, in obviously serious condition. There had been no vomiting in the interval, but she had become progressively weaker, losing the use of her legs almost entirely and to a less extent the use of her hands. Mental changes had become more pronounced, so that at times she was almost completely disoriented and also had auditory hallucinations. Examination showed no loss of weight. Definite though not deep jaundice present. Blood pressure 120/88, temperature 37° C., pulse 110. Urine showed a trace of albumin with numerous casts and white blood cells. Fundus palpable at level of umbilicus. Liver edge palpable 3 cm. below costal margin. A slight degree of secondary anemia was now present, hemoglobin (Sahli) 82 per cent, R.B.C. 3,550,000, W.B.C. 9,200. No edema present. The neurologic findings were of interest. She appeared dull and apathetic and was disoriented as to time, but particularly as to place and person, with definite memory impairment for recent events. Admits auditory hallucinations but no visual ones. Cranial nerves negative except for slight nystagmoid movements. There were no localized atrophies or deformities. Upper extremities showed weakness but no actual paralysis. The biceps and triceps reflexes were absent, also the umbilical reflex. The lower extremities also showed definite weakness though no actual paralysis. The knee and Achilles reflexes were absent, and the sense of motion of the toes was lost. Marked tenderness was present along the nerve trunks of the lower extremities. She complained of numbness of hands and forearms, but there were no objective sensory changes.

Diagnosis: Toxic polyneuritis and psychosis.

She was placed on a low protein diet with forced fluids, taking these very well for the first two days, the intake being 3,000 c.c. and 2,100 c.c. respectively. The output of urine was apparently rather scanty though it could not be accurately measured on account of incontinence from time to time. The only medication made use of was barbital and paraldehyde occasionally to promote sleep and to quiet her occasional periods of mental excitement. She vomited twice, but vomiting was not a feature of the clinical picture. During the first two days in the hospital, her general condition showed little change, but in the following two days her condition became much worse. The fluid intake decreased so that the intravenous administration of glucose was resorted to, the jaundice became somewhat more pronounced, and mentally she became very torpid. Evidence of progressive paralysis of the extremities appeared. She presented the appearance of an extremely ill woman, and it was felt that her best chance of recovery lay in terminating the pregnancy. This was done on November 1 by vaginal hysterotomy under nitrous oxide

and oxygen anesthesia, the fetus weighing 310 gm. and measuring 26.5 cm. in length.

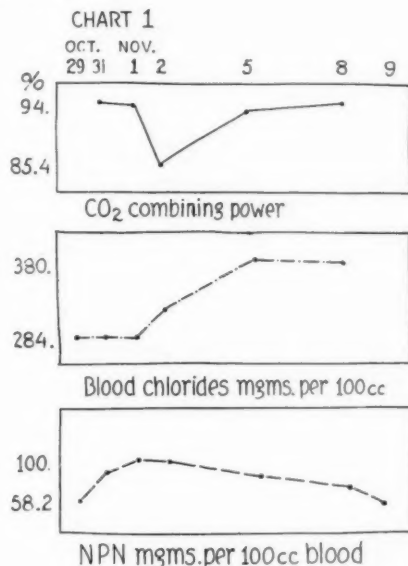
For the first few days postoperative, she showed some improvement. The urinary output increased, though it was still impossible to determine this accurately on account of periodic incontinence. The jaundice was rather less marked and she took fluids well by mouth with no vomiting. The mental state improved somewhat though the paralysis became more marked with almost complete flaccid paralysis of both lower extremities, bilateral wrist and foot drop, and complete absence of reflexes. The urine continued to show a trace of albumin with numerous hyaline and granular casts, white blood cells, and colon bacilli present.

The chemical studies made on the blood both before and after operation presented a number of findings of very considerable interest, showing a high nonprotein nitrogen and uric acid content, and low chlorides with a very high CO_2 combining power.

		N.P.N.	UR. AC.	CL.	SUGAR	CO_2
*Before operation	Oct. 29	58.2 mg. per 100 c.c.	—	—	94.3	—
	Oct. 31	87	11.5	284	105	94 %
	Nov. 1	100	12.3	284	100	93.8
After operation	Nov. 2	98	12.5	320	110	85.4
	Nov. 5	75	9.2	380	133	92.2
	Nov. 8	57.2	6.6	380	111	93

*In these determinations, the CO_2 combining power was estimated on the plasma, the other observations were on oxalated whole blood.

A single observation on the urine (reaction acid) prior to operation showed an ammonia coefficient of 5.7 per cent.



On account of the profound disturbance of metabolism which was obviously present, a number of other investigations were carried out which resulted in several findings of considerable interest. In view of the high CO_2 combining power, indicating changes in the nature of an alkalosis, the P_{H} of the blood was determined. This determination was made by McQuarrie, by his method, and the reading on November 3 was 7.42. This is regarded as the very upper limit of normal, and it is possible that had a specimen been taken twenty-four hours earlier it might have shown a marked degree of alkalinity. Repeated on November 9, the reading was 7.37.

On November 3, the same day as the first P_H determination was made, the fatty acids of the blood were determined by Dr. W. R. Bloor with the following result:

Cholesterol	61 mg. per 100 c.c. plasma (approximately half normal)
Total fatty acids	700 mg. per 100 c.c. plasma (nearly twice normal)
Phospholipids	218 mg. per 100 c.c. plasma (normal)

The spinal fluid on November 9 showed:

N.P.N.	35.3 mg. per 100 c.c.
Chlorides	660 mg. per 100 c.c.
Sugar	71.4 mg. per 100 c.c.
P_H	7.37

The Vandenberg reaction on blood showed:

Nov. 1	4.5 units bilirubin
Nov. 2	2 units bilirubin
Nov. 8	less than 1 bilirubin
Nov. 5	blood calcium, 9 mg. per 100 c.c.
	blood phosphates 4 mg. per 100 c.c.

These latter are both normal figures and the observations were not repeated.

After the slight improvement noted during the first two or three days postoperative, the patient's condition grew steadily worse. She became progressively weaker, paralysis became more pronounced, until it was finally almost complete, while her mental state was unimproved.

After the fourth day postoperative she showed a slight daily rise of temperature to 38° or 38.5° C. The urine (always acid in reaction) showed constantly numerous white blood cells and colon bacilli, these being present from the time of her second admission. There was undoubtedly some infection of the urinary tract present, though it did not form a prominent feature of the clinical picture.

The patient died on the eleventh day postoperative, apparently as a result of respiratory failure; possibly involvement of the phrenic nerves may have played a part. Unfortunately no autopsy could be obtained.

CASE 2.—(Unit No. 22465) A twenty-year-old woman in her first pregnancy, admitted March 6, 1929, complaining of weakness, loss of weight, and deafness. The date of the last menstrual period was unreliable being given as September 16 and December 15 preceding admission. From subsequent findings the former is probably the correct date. The pregnancy was uneventful except for a slight respiratory infection of a few days duration in October. About the middle of December she began to vomit occasionally, the vomiting becoming persistent, and in six weeks she lost about 35 pounds in weight. For the two weeks prior to her admission vomiting was not a prominent symptom however. During the past two weeks her hearing had become quite defective. It was noticed that she tended to make irrelevant remarks and at times was quite drowsy. One week before admission she began to notice weakness of the legs and impairment of locomotion.

Examination revealed a poorly nourished woman, weight 32.2 kilos; temperature 37° C.; pulse 78; respirations 20; blood pressure 90/60. Some degree of secondary anemia, hemoglobin 75 per cent; R.B.C. 4,020,000; W.B.C. 7,950. No jaundice. Wassermann negative. Urine showed both acetone and diacetic acid but no other abnormal findings. Pelvic examination showed the uterus to be a size slightly larger than a three months' pregnancy. (This was too small for the period of amenorrhea if the last menstrual period occurred in September, but at this time the exact date was not known.)

Lumbar puncture failed to obtain any fluid though the canal was definitely entered. Neurologic examination revealed a mild mental confusion and defective memory with disorientation as to time, but not as to place and person. Examination of the cranial nerves showed advanced nerve deafness, both auditory nerves being involved, and also well marked nystagmus. The upper extremities showed no neurologic abnormalities, but there was marked weakness of the lower extremities, with absent knee jerks and diminished Achilles reflexes. She was unable to walk without assistance and the gait showed weakness and ataxia.

Diagnosis: Toxic polyneuritis and psychosis.

She was placed on a high carbohydrate diet with forced fluids on which she did very well for the first twenty-four hours, although there was occasional vomiting. She was also given glucose and normal saline intravenously. It was impossible to estimate the urinary output on account of incontinence.

During the next two days her condition became much worse with more pronounced mental disturbance and progressive paralysis. Vomiting was not a feature, but on account of inability to cooperate, fluid administration became entirely dependent upon intravenous glucose and saline.

On account of her rather rapid course, the pregnancy was terminated on March 9, three days after admission, by dilatation of the cervix followed by removal of the ovum, nitrous oxide and oxygen anesthesia being used. When the uterus was emptied, a dead ovum representing an approximately three and one-half months' pregnancy was obtained. The embryo was mummified, and the placenta markedly infarcted though microscopic examination of the latter revealed syncytial cells that were apparently still active. From the findings and menstrual history, it would appear that the symptoms began shortly before the death of the ovum, though it is impossible to be specific in regard to this. We assume that the pregnancy began in September, and that death of the ovum occurred three months or so later, the dead ovum being retained until it was removed at operation.

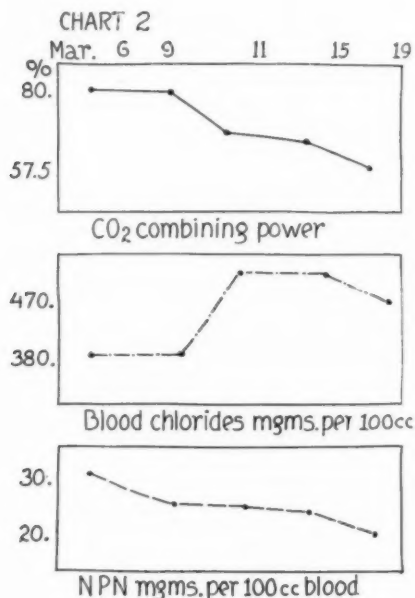
For several days following operation there was definite improvement. She took fluids fairly well by mouth and in addition was given glucose and normal saline intravenously. The urinary output improved materially though accurate measurements were still impossible on account of incontinence; acetone and diacetic acid disappeared from the urine. The hearing returned to practically normal. The paralysis persisted however, and after the first few days post-operative, became progressive involving both upper and lower extremities.

In spite of the fact that she lost only a small amount of blood at operation, she developed a marked degree of secondary anemia and on the ninth day post-operative, the hemoglobin was 45 per cent and the R.B.C. 2,600,000. She was therefore given transfusions of 500 c.c. of citrated blood on two occasions.

Such improvement as was noted immediately postoperative proved to be of a very temporary nature. She became much worse on the eleventh day postoperative, with extreme prostration, almost complete paralysis, and died on March 21, 1929, the thirteenth day after termination of the pregnancy. She never developed any jaundice. Autopsy obtained.

The following results were obtained from the chemical examination of the blood at various times: Vandenberg—2.0 units bilirubin.

			N.P.N.	UR. AC. CL.	SUGAR	CO ₂	CA.	PHOSPH.	
Before operation	{	March 6	30 mg. per 100 c.c.	5	380	80	80%	11.6	3.4
		March 9	24 mg. per 100 c.c.	—	380	80	80%	10	3.3
After operation	{	March 11	23 mg. per 100 c.c.	—	500	100	66%	—	—
		March 15	24 mg. per 100 c.c.	—	500	80	61%	—	—
		March 19	20 mg. per 100 c.c.	—	470	85	57.5%	—	—



Urine obtained the day before operation showed an ammonia coefficient of 8.75 per cent (reaction acid). No other determinations of this were made on account of unsatisfactory collections.

The spinal fluid obtained at the time of operation showed the chloride content to be 575 mg. per 100 c.c. The P_{H_2} of the spinal fluid was 7.30 (upper limit of normal), the blood obtained the same day showed a CO_2 combining power of 80 per cent. The CO_2 content of the spinal fluid was 62.1 mg. per 100 c.c.

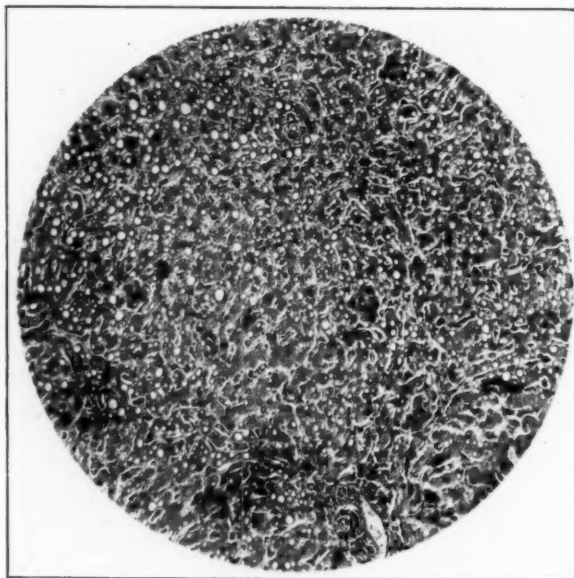


Fig. 1.—Microphotograph of liver from Case 2 showing extensive fatty infiltration. Not a characteristic lesion.

Autopsy Findings.—Liver: Weight 1,250 gm. No gross or microscopic areas of necrosis. Definite fatty infiltration is present. (This cannot be regarded as specific.) See Fig. 1.

Kidneys: Normal except for one microscopic area of polymorph infiltration in the parenchyma.

Lungs: A few early patches of bronchopneumonia.

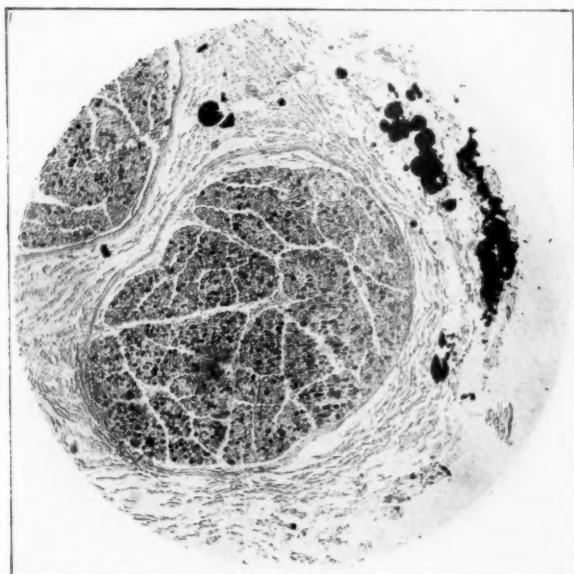


Fig. 2.—Microphotograph of cross section of radial nerve stained by the Marchi method showing areas of degeneration.

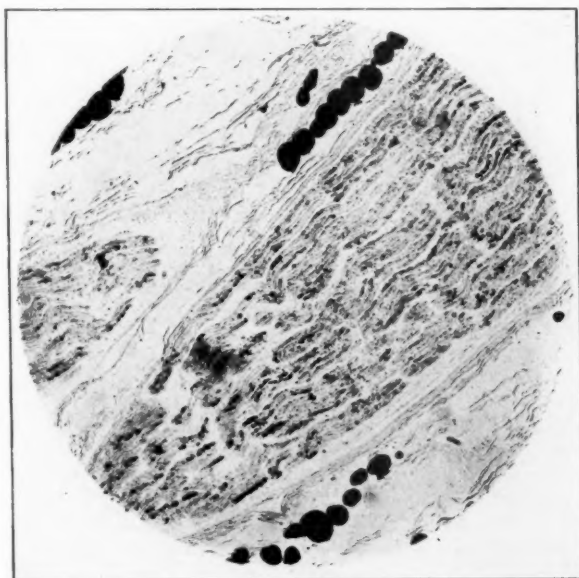


Fig. 3.—Microphotograph of longitudinal section of sciatic nerve stained by the Marchi method showing areas of degeneration.

Brain and Spinal Cord: Sections stained with Nissl's and Weigert's iron hematoxylin stains showed no pathology.

Peripheral Nerves: Sections of the peripheral nerves, including the sciatic, ulnar, and radial, stained by the Marchi method showed well marked peripheral neuritis of the toxic type. See Figs. 2 and 3.

No other findings of significance were noted.

CASE 3.—(Unit No. 25599) A thirty-year-old woman, admitted June 20, 1929, on account of a confused mental state which had developed four or five days previously. Three weeks previously a pregnancy of three months' duration had been terminated at another hospital on account of persistent vomiting. So far as is known, the operation was not followed by any infection, and vomiting ceased after interruption of the pregnancy. Up to the time of the termination of the pregnancy there had been no mental disturbance and no paralysis, but there had been hyperesthesia of the hands and feet. A wrist drop developed three days after operation.

Examination: Temperature 37.5; respirations 22; pulse 128; blood pressure 120/110. Sclerae jaundiced; Wassermann negative; urine negative. She showed evidence of some loss of weight. No other points of interest were noted except the neurologic findings which were as follows: The patient was highly emotional, and partially disoriented with impairment of memory for recent events. Cranial nerves negative except for some nystagmus. Weakness of both upper extremities with bilateral wrist drop, the biceps reflexes being diminished and the triceps and radial reflexes absent. The nerve trunks of the upper extremities were very sensitive to deep pressure and the dorsal interossei muscles of the hands showed definite atrophy. The lower extremities showed marked weakness and limitation of movement with bilateral foot-drop, the nerve trunks being markedly sensitive to pressure. Knee and Achilles reflexes absent. Marked hyperesthesia and hyperalgesia in both upper and lower extremities.

Diagnosis: Toxic polyneuritis and psychosis.

Physiotherapy treatments resulted in some improvement of muscular movements. The mental symptoms varied considerably, and at times she was completely disoriented and presented visual hallucinations and delusions, but five weeks after admission her mental state was practically normal.

On June 25th the following findings were noted on chemical study of the blood.

Sugar	101.5 mg. per 100 c.c.
Calcium	11.8 mg. per 100 c.c.
Chlorides	464 mg. per 100 c.c.
N.P.N.	35.9 mg. per 100 c.c.
CO ₂	58.1%

The spinal fluid showed a P_H of 7.32. There was not a profound disturbance of metabolism present such as was noted in the other two patients.

She was discharged from the hospital on September 1, 1929, against advice, her mental condition normal, residual paralysis of both lower and upper extremities still present, though the lower extremities showed quite marked improvement. Banjo splints were applied to the hands, and arrangements were made to continue physiotherapy with baking and massage at her home.

When seen on September 25, 1929, the condition of the extremities was not as good, marked atrophy now being present. She was not seen again by us, and died on November 29, 1929. It was learned that after she left the hospital she had rather persistent vomiting for three or four weeks, but this ceased entirely about four weeks before her death. No further mental disturbance developed, and she was able to take a few steps shortly before she died. She was jaundiced for a few days before death, and it was said that profound weakness, drowsiness, and stupor without edema or convulsions preceded her death.

SUMMARY AND DISCUSSION

Three cases are presented, the patients showing signs of extensive polyneuritis associated with pregnancy. There was also a profound mental disturbance in each instance, and at the onset of the illness severe and persistent vomiting. We feel that we have satisfactorily excluded such toxic agents as alcohol, and lead, and also infection as possible etiologic factors, and feel justified therefore in ascribing the origin to a toxemic process associated with pregnancy. It is impossible to make any definite statements in regard to the exact etiology, and for the present, the condition must remain in the category of unsolved problems in common with the other toxemias of pregnancy.

While this acute form is an unusual complication of pregnancy, it is an extremely serious one, and carries with it a high mortality.

In two of our patients, there was associated a profound disturbance of the general metabolism, characterized particularly by a high CO_2 combining power and low blood chlorides. The findings are those of an alkalosis, yet inasmuch as the P_H in each instance fell within normal limits, one must regard the condition present as a compensated alkalosis. In Case 3, no profound change in metabolism was noted, yet with a CO_2 combining power of 58.1 per cent and blood chlorides of 464 mg., there was at least a tendency in a similar direction, and quite possibly similar changes might have been found if we had had the opportunity to study her during the earlier stages of her illness.

It is interesting to speculate on the possible factors causing this type of disturbance. None of these women had had any alkaline medication during their illness. None showed any appreciable respiratory disturbance. All had had severe and persistent vomiting prior to admission. This vomiting, with the associated loss of hydrochloric acid may be a possible factor. Stander has observed a few instances of transient alkalosis in cases of pernicious vomiting which could apparently be attributed to this factor, but it was only a transient phenomenon. At the time the patients in Cases 1 and 2 were under observation in the hospital, it is true that occasional vomiting occurred, but it was not at all a prominent feature of the clinical picture, and had the alkalosis been caused by the severe vomiting which had occurred some weeks previously, and had this been the only factor, one would expect that complete adjustment would have taken place by the time of admission. Of course, in the presence of defective elimination, alkali might well be retained, and the CO_2 then would remain high. In Case 1 there evidently was retention, and the nonprotein nitrogen readings were consistently higher than normal, and yet with improved elimination before death and a marked drop in the nonprotein nitrogen the CO_2 combining power remained as high as ever.

In Case 2 with no evidence of retention the CO_2 combining power was high and did not approach a normal figure for more than a week after admission. Therefore while recognizing the possibility that the

vomiting may have been the important factor in the causation of the metabolic disturbances noted, yet we feel that there is sufficient evidence to suggest that it was not the sole factor and that other unknown conditions may have played a part in the production of these changes.

In Case 2 the association of the illness with a dead ovum (missed abortion) is also of interest. When the ovum was removed at operation, it had obviously perished some weeks previously, and yet as noted previously, microscopic examination did reveal some syncytial cells which were undoubtedly still living. Whether they played a part in the causation of the toxemia, or whether this had been inaugurated before the death of the ovum, continuing its acute course in spite of this fact, it is impossible to say, though the latter situation is the more probable. Under the circumstances present it is very questionable as to whether termination of the pregnancy did any good in this instance.

In regard to treatment, we have little to suggest. The exact etiology of the condition being unknown, treatment can obviously only be along general lines. In the presence of persistent vomiting, the administration of fluids, saline, and glucose by various methods would appear logical, as in the treatment of pernicious vomiting. With the possible presence of an alkalosis, alkalis should assuredly not be given.

As to whether the pregnancy should be terminated and if so when, we find it impossible to be specific.

In our Cases 1 and 2, there was some temporary improvement following the termination of the pregnancy, but this was only temporary. In our Case 3, the pregnancy had been terminated before the occurrence of mental symptoms, and in what probably represented the early stages of the peripheral nerve involvement, yet in spite of this the course was not arrested, though the vomiting ceased. Furthermore, a number of the recorded cases have shown the first symptoms in the puerperium, some days or longer after the pregnancy had come to an end.

With these observations in mind it is apparent that termination of the pregnancy will not necessarily result in the cure of the condition. Furthermore, as noted by Von Hösslin, many will recover without interruption of the pregnancy. On the other hand if the individual's natural resistance to the toxic process is not sufficient, or if she fails to respond to general measures, there would seem to be little else left to do, also as Seitz suggests in the event of involvement of the optic or phrenic nerves.

Treatment of the affected peripheral nerves, will be along the usual lines for such lesions arising from other causes and in the event of permanent disability, orthopedic appliances may become necessary.

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THE INFLUENCE OF AGE AND COLOR ON THE MATERNAL AND FETAL DEATH RATE

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IN A preceding communication, we have dealt with the age incidence in a large number of women delivered consecutively on the Obstetrical Service of the Johns Hopkins Hospital, and have discussed the influence of age on the type of delivery. Following this, it has seemed important to investigate the maternal and fetal death rate as influenced by the race of the mother, as well as by her age at the time of delivery.

For this purpose, we have used the same series of cases as in the former investigation, i. e. 15,370 consecutive deliveries, premature and full-term, during the period from January 1, 1907, to December 31, 1929. The material is almost equally divided between whites and blacks, primiparae and multiparae, as may be seen from Table I, from which twelve cases have been omitted because of lack of sufficient data.

TABLE I.

	WHITE	BLACK	TOTAL
Primiparae	4057	4347	8404
Multiparae	3738	3216	6954
Total	7795	7563	15,358

Tables II and III show the distribution of maternal deaths according to age, race, and parity in the entire series, together with the mortality percentage in each group. There were in all 121 deaths, a gross maternal mortality of 0.79 per cent. The death rate was higher among the black than the white women, being 0.94 and 0.64 per cent, respectively. It will be noted that the death rates are consistently higher in the black than in the white race when the cases are divided not only according to parity but also according to type of delivery. At first glance many of these racial differences seem small. Their significance has, however, been tested statistically by dividing each difference by its standard deviation, and from the quotient obtained, computing the probability of such an observed difference being the result of chance or of a sampling error. The results of these tests are shown in Table VIII.

It will be noted that the death rate in each type of delivery is higher in multiparae than in primiparae. As has been stated before, we con-

sider the primiparous population in this series of cases as fairly representative and normal. However, the multiparae contain a disproportionate number of referred emergency cases, and a decreased number of normal women, which to some extent accounts for the observed difference. Nevertheless, we believe that in a normal population similar conditions

TABLE II. MATERNAL DEATHS, ACCORDING TO RACE, AGE, AND PARITY*

	AGE - 16		17 - 19		20 - 24		25 - 29		30 - 34		35 - 39		40 -		TOTAL	
	TOTAL DELIV.	MAT. DEATHS	TOTAL DELIV.	MAT. DEATHS	TOTAL DELIV.	MAT. DEATHS	TOTAL DELIV.	MAT. DEATHS	TOTAL DELIV.	MAT. DEATHS	TOTAL DELIV.	MAT. DEATHS	TOTAL DELIV.	MAT. DEATHS	TOTAL DELIV.	MAT. DEATHS
White para 0	299	2	1347	2	1649	7	489	4	172	0	80	3	21	0	4057	18
Black para 0	806	6	1976	10	1180	10	269	4	75	1	37	0	4	0	4347	31
White para x	5	0	202	1	1007	3	1037	6	797	9	491	7	199	6	3738	32
Black para x	28	0	507	4	1244	11	737	6	373	9	242	8	85	2	3216	40
Total para 0	1105	8	3323	12	2829	17	758	8	247	1	117	3	25	0	8404	49
Total para x	33	0	709	5	2251	14	1774	12	1170	18	733	15	284	8	6954	72
Total white	304	2	1549	3	2656	10	1526	10	969	9	571	10	220	6	7795	50
Total black	834	6	2483	14	2424	21	1006	10	448	10	279	8	89	2	7563	71
Total pts.	1138	8	4032	17	5080	31	2532	20	1417	19	850	18	309	8	15,358	121

*Deliv., deliveries. Mat., maternal.

MATERNAL MORTALITY PERCENTAGE

	-16	17-19	20-24	25-29	30-34	35-39	40-	TOTAL
White para 0	0.67	0.15	0.42	0.82	—→	1.10	←—	0.44
Black para 0	0.74	0.51	0.85	1.49	—→	0.86	←—	0.71
White para x	—→0.48←—		0.30	0.58	1.13	1.43	3.02	0.86
Black para x	—→0.75←—		0.88	0.81	2.41	3.31	2.35	1.24
Total para 0	0.72	0.36	0.60	1.06	—→	1.03	←—	0.58
Total para x	—→0.67←—		0.62	0.68	1.54	2.05	2.82	1.04
Total white	0.66	0.19	0.38	0.66	0.93	1.75	2.73	0.64
Total black	0.72	0.56	0.87	0.99	2.23	2.87	2.25	0.94
Total pts.	0.70	0.42	0.61	0.79	1.34	2.12	2.59	0.79

*Deliv., deliveries. Mat., maternal.

would be observed, though to a lesser extent, owing to the increased number of obstetric complications to which the multipara is subject.

It will be observed that in both whites and blacks, primiparae and multiparae, the death rate is lowest in women delivered spontaneously at term, rises definitely with operative delivery, and is highest in premature births. Since in many cases the premature delivery is due to some grave obstetric complication, the latter finding is not surprising. Furthermore, the increased mortality of operative over spontaneous delivery is significant, and gives added force to the arguments of those advocating more conservative methods of obstetrics throughout the country, as well as more intelligent care of abnormal cases.

TABLE III. MATERNAL MORTALITY PERCENTAGES

	PER CENT
Total cases, both races	0.79
Total cases, white	0.64
Total cases, black	0.94
Total primiparae, both races	0.58
Total multiparae, both races	1.04
Total primiparae, white	0.44
Total primiparae, black	0.71
Total multiparae, white	0.86
Total multiparae, black	1.24
Total full-term spontaneous deliveries	0.21
Total full-term operative deliveries	2.12
Total premature deliveries	3.90
Full-term spontaneous, white	0.19
Full-term operative, white	1.86
Premature, white	2.96
Full-term spontaneous, black	0.24
Full-term operative, black	2.44
Premature, black	4.48
Full-term spontaneous, white primiparae	0.07
Full-term spontaneous, black primiparae	0.18
Full-term spontaneous, white multiparae	0.30
Full-term spontaneous, black multiparae	0.33
Full-term operative, white primiparae	1.28
Full-term operative, black primiparae	1.73
Full-term operative, white multiparae	2.81
Full-term operative, black multiparae	3.36
Premature, white primiparae	2.23
Premature, black primiparae	4.19
Premature, white multiparae	3.65
Premature, black multiparae	4.78

In each rubric of Tables II and III the mortality is higher among the blacks than the whites. Tested statistically some of these differences are highly significant, while others mean little. However, since all these differences, even though small, show the higher mortality to be on the side of the black race, one is safe in asserting that women of that race throughout their obstetric career are significantly poorer risks than are the white.

Table II indicates the mortality differences according to age. A study of this Table II indicates that the young woman of 16 years or less is not an ideal obstetric subject, and shows that the optimum age for child-bearing is between 17 and 19 years, inclusive. From then onward, there is a trend upward in the mortality rate, which rises rapidly as the older age groups are reached.

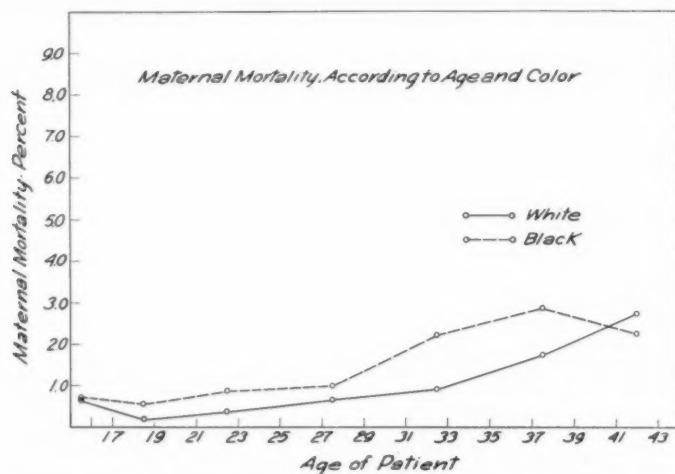


Fig. 1.—Indicating the higher maternal mortality among the black race. In both races the mortality increases with age.

Table IV sets forth the causes of death in the 121 women who succumbed in this series. Infection, toxemia, and hemorrhage, the three chief causes of death among obstetric patients, account for 64.46 per cent or about two-thirds of the total number. Infection, which in most statistics accounts for more deaths than any other cause, yields precedence to toxemia in our series. Moreover, it will be noted that only 6 of the 27 deaths due to infection occurred in white women. Consequently, the experience in this service indicates that the colored woman is not only more prone to become infected than the white, but is also less able to combat the infection once it has made its appearance.

Table IV A indicates the mortality rate among the patients in this series expressed in terms of 10,000 deliveries. In both races the maternal mortality from infection is higher in multiparous than in primiparous women. In white women toxemia accounts for approximately two-fifths of the mortality, while only one-eighth of the deaths are due to infection. Among the colored women, on the other hand, toxemia and infection account for almost one-fifth and one-third of the total deaths, respectively. Deaths due to hemorrhage are about equally divided in the two races. From our observation, it would seem that the higher mortality observed in the black race is due chiefly to a death rate from infection which is almost four times greater than in the white.

TABLE IV. CAUSES OF MATERNAL DEATHS

	WHITE			BLACK			TOTAL
	PARA 0	PARA X	TOTAL	PARA 0	PARA X	TOTAL	
<i>Group 1. Infection</i>							
22.31 Per Cent of Total Deaths							
1. Infection	2	4	6	9	12	21	27
<i>Group 2. Toxemia</i>							
28.10 Per Cent of Total Deaths							
1. Eclampsia	8	4	12	6	7	13	25
2. Nephritis	2	5	7	1	1	2	9
<i>Group 3. Hemorrhage</i>							
14.05 Per Cent of Total Deaths							
1. Placenta previa	0	5	5	0	2	2	7
2. Premature separation placenta	0	2	2	1	2	3	5
3. Postpartum hemorrhage	0	2	2	2	1	3	5
<i>Group 4. Other Obstetric Causes</i>							
18.18 Per Cent of Total Deaths							
1. Rupture of uterus	0	1	1	0	5	5	6
2. Embolus	1	2	3	1	1	2	5
3. Chloroform poisoning	1	0	1	1	1	2	3
4. Anesthesia	0	0	0	2	0	2	2
5. Cardiac	0	1	1	1	0	1	2
6. Extrauterine pregnancy	0	0	0	1	0	1	1
7. Other	2	0	2	1	0	1	3
<i>Group 5. Nonobstetric Causes</i>							
17.36 Per Cent of Total Deaths							
1. Lobar pneumonia	1	5	6	2	5	7	13
2. Tuberculosis	0	1	1	2	2	4	5
3. Other	1	0	1	1	1	2	3
Totals	18	32	50	31	40	71	121

TABLE IV A. DEATHS OF OBSTETRIC PATIENTS FOR 10,000 DELIVERIES, ACCORDING TO CAUSE OF DEATH

	WHITE			BLACK			TOTAL
	PARA 0	PARA X	TOTAL	PARA 0	PARA X	TOTAL	
Infection	4.9	10.7	7.7	20.7	37.3	27.8	17.6
Toxemia	24.6	24.1	24.4	16.1	24.9	19.8	22.1
Hemorrhage	0.0	24.1	11.5	6.9	15.5	10.6	11.1
Other Obstetric Causes	9.9	10.7	10.3	16.1	21.8	18.5	14.3
Nonobstetric causes	4.9	16.1	10.3	11.5	24.9	17.2	13.7
Total	44.3	85.7	64.2	71.3	124.4	93.9	78.8

Turning now to a consideration of fetal mortality, Table V indicates the stillborn and neonatal deaths observed in this series, according to race, age, and parity, together with the mortality percentage in each category. Again, a higher rate is found throughout in the black race, and one sufficiently higher to be in most cases extremely significant. As

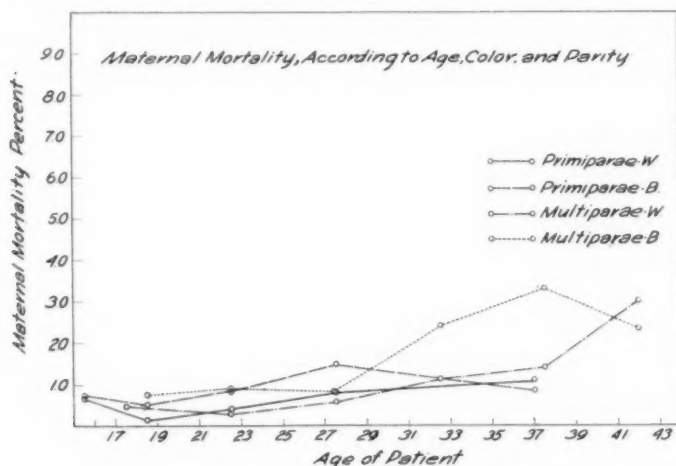


Fig. 2.—Indicating the higher mortality among multiparae. The "young primipara" has a higher mortality rate than does the woman of seventeen to twenty-five years.

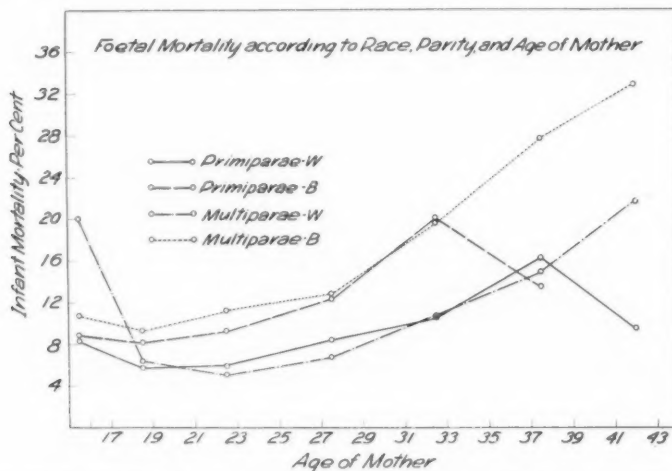


Fig. 3.—Indicating a relatively high fetal mortality below the age of seventeen, an optimum from seventeen to nineteen, and a steady rise from the age of twenty, becoming great as the older age groups are reached.

was observed in the discussion of maternal deaths, the fetal rate is higher among the multiparous than the primiparous women. The abnormal population in the former group probably accounts for a considerable part of this observed difference. A relatively high mortality is again noted among the young women; and this is particularly true in the case of the "young primipara." The black woman seems correspondingly

less affected by extreme youth than does the white. Again we find a rapidly rising mortality percentage in the later age groups, both in primiparae and multiparae. Here the abnormal population factor among the multiparae would seem to have little influence on the trend of the death rate, and we believe that this finding is significant.

TABLE V. TOTAL FETAL DEATHS, ACCORDING TO AGE, RACE AND PARITY

	AGE - 16		17 - 19		20 - 24		25 - 29		30 - 34		35 - 39		40 -		TOTAL	
	TOTAL DELIV.	FETAL DEATHS	TOTAL DELIV.	FETAL DEATHS	TOTAL DELIV.	FETAL DEATHS	TOTAL DELIV.	FETAL DEATHS	TOTAL DELIV.	FETAL DEATHS	TOTAL DELIV.	FETAL DEATHS	TOTAL DELIV.	FETAL DEATHS	TOTAL DELIV.	FETAL DEATHS
White para 0	299	24	1347	78	1649	98	489	41	172	18	80	13	21	2	4057	274
Black para 0	806	72	1976	163	1180	109	269	33	75	15	37	5	4	0	4347	397
White para x	5	1	202	13	1007	51	1037	71	797	85	491	73	199	43	3738	337
Black para x	28	3	507	47	1244	139	737	94	373	73	242	67	85	28	3216	451
Total para 0	1105	96	3323	241	2829	207	758	74	247	33	117	18	25	2	8404	671
Total para x	33	4	709	60	2251	190	1774	165	1170	158	733	140	284	71	6954	790
Total white	304	25	1549	91	2656	149	1526	112	969	103	571	86	220	45	7795	613
Total black	834	75	2483	210	2424	248	1006	127	448	88	279	72	89	28	7563	848
Total pts.	1138	100	4032	301	5080	397	2532	239	1417	191	850	158	309	73	15,358	1461

FETAL MORTALITY PERCENTAGE

AGE	-16	17-19	20-24	25-29	30-34	35-39	40-	TOTAL
White para 0	8.03	5.79	5.94	8.38	10.47	→14.85←		6.75
Black para 0	8.93	8.25	9.24	12.27	20.00	→12.20←		9.13
White para x	→6.76←		5.06	6.85	10.92	14.87	21.61	9.07
Black para x	→9.35←		11.17	12.75	19.57	27.69	32.94	14.02
Total para 0	8.69	7.25	7.32	9.76	13.36	→14.08←		7.98
Total para x	→8.63←		8.44	9.30	13.50	19.10	25.00	11.36
Total white	8.22	5.87	5.61	7.34	10.63	15.06	20.45	7.86
Total black	8.99	8.46	10.23	12.62	19.64	25.81	31.46	11.21
Total pts.	8.79	7.47	7.81	9.44	13.48	18.59	23.62	9.51

TABLE VI. TOTAL FETAL DEATHS AT TERM ACCORDING TO AGE, RACE, AND PARITY

	AGE - 16		17 - 19		20 - 24		25 - 29		30 - 34		35 - 39		40 -		TOTAL
	TOTAL DELIV.	FETAL DEATHS	TOTAL DELIV.	FETAL DEATHS	TOTAL DELIV.	FETAL DEATHS	TOTAL DELIV.	FETAL DEATHS	TOTAL DELIV.	FETAL DEATHS	TOTAL DELIV.	FETAL DEATHS	TOTAL DELIV.	FETAL DEATHS	
White para 0	285	16	1276	40	1579	72	474	35	169	15	74	8	21	2	3878 187
Black para 0	745	46	1841	102	1097	67	247	21	67	10	36	5	4	0	4037 251
White para x	5	1	193	8	962	26	994	47	755	51	458	48	181	31	3548 210
Black para x	23	1	459	27	1150	79	673	48	338	49	207	41	73	17	2923 262
Total para 0	1030	62	3117	142	2676	139	721	55	236	25	110	13	25	2	7915 438
Total para x	28	2	652	35	2112	105	1667	93	1093	100	665	89	254	48	6471 472
Total white	290	17	1469	48	2541	98	1468	79	924	66	532	56	202	33	7426 397
Total black	768	47	2300	129	2247	146	920	69	405	59	243	46	77	17	6960 513
Total pts.	1058	64	3769	177	4788	244	2388	148	1329	125	775	102	279	50	14,386 910

FETAL MORTALITY PERCENTAGE

AGE	-16	17-19	20-24	25-29	30-34	35-39	40-	TOTAL
White para 0	5.61	3.13	4.56	7.17	8.88	→10.53←		4.82
Black para 0	6.17	5.54	6.11	8.50	14.93	→12.50←		6.22
White para x	→4.57←		2.70	4.53	6.75	10.48	17.13	5.92
Black para x	→5.81←		6.87	7.13	14.50	19.81	23.29	8.96
Total para 0	6.02	4.55	5.19	7.63	10.59	→11.11←		5.53
Total para x	→5.44←		4.97	5.58	9.15	13.38	18.90	7.29
Total white	5.86	3.27	3.86	5.38	7.14	10.53	16.34	5.35
Total black	6.12	5.61	6.50	7.50	14.57	18.93	22.08	7.37
Total pts.	6.05	4.70	5.10	6.20	9.41	13.16	17.92	6.33

The total fetal mortality is 9.51 per cent. This rather high figure is due to the presence of many premature labors in the series and in Table VI only those children born at or near term (2500 grams and over) are included, whereby the mortality is decreased to 6.33 per cent. The total mortality rates are of course considerably lower in this table than

TABLE VII. FETAL MORTALITY ACCORDING TO TYPE OF DELIVERY

	FULL-TERM SPONTANEOUS			FULL-TERM OPERATIVE			PREMATURE		
	TOTAL DELIV.	FETAL DEATHS	MORTALITY PER CENT	TOTAL DELIV.	FETAL DEATHS	MORTALITY PER CENT	TOTAL DELIV.	FETAL DEATHS	MORTALITY PER CENT
White para 0	2942	75	2.55	936	112	11.97	179	87	48.60
Black para 0	3344	101	3.02	693	150	21.65	310	146	47.10
White para x	2981	85	2.85	567	125	22.05	190	127	66.84
Black para x	2388	126	5.28	535	136	25.42	293	189	64.51
Total para 0	6286	176	2.80	1629	262	16.08	489	233	47.65
Total para x	5369	211	3.93	1102	261	23.68	483	316	65.42
Total white	5923	160	2.70	1503	237	15.77	369	214	57.99
Total black	5732	227	3.96	1228	286	23.29	603	335	55.56
Total pts.	11,655	387	3.32	2731	523	19.15	972	549	56.48

TABLE VIII. SIGNIFICANCE OF DIFFERENCES IN MATERNAL AND FETAL MORTALITY, ACCORDING TO RACE AND PARITY

	DIFF.	DIFF. σ DIFF.	P. ¹
<i>Maternal Mortality</i>			
Total cases, white vs. black	0.0030	2.10	35.8 in 1000
Primiparae, white vs. black	0.0027	1.62	105.2 in 1000
Multiparae, white vs. black	0.0038	1.54	123.6 in 1000
Full-term spontaneous, white vs. black	0.0005	0.58	562.0 in 1000
Full-term operative, white vs. black	0.0058	1.03	303.0 in 1000
Premature, white vs. black	0.0152	1.25	211.2 in 1000
F.T.S. para O, white vs. black	0.0011	1.25	211.2 in 1000
F.T.O. para O, white vs. black	0.0045	0.73	456.4 in 1000
Premature para O, white vs. black	0.0196	1.24	215.0 in 1000
F.T.S. para X, white vs. black	0.0003	0.19	849.4 in 1000
F.T.O. para X, white vs. black	0.0055	0.54	589.2 in 1000
Premature para X, white vs. black	0.0113	0.61	541.8 in 1000
White para O vs. para X	0.0042	2.33	19.8 in 1000
Black para O vs. para X	0.0053	2.27	23.2 in 1000
Total cases para O vs. para X	0.0046	3.13	1.8 in 1000
<i>Fetal Mortality</i>			
Total cases, white vs. black	0.0335	7.07	1 in 1000
Primiparae, white vs. black	0.0238	4.05	1 in 1000
Multiparae, white vs. black	0.0495	6.41	1 in 1000
Full-term spontaneous, white vs. black	0.0126	3.78	1.2 in 1000
Full-term operative, white vs. black	0.0752	4.92	1 in 1000
Premature, white vs. black	0.0243	0.74	459.4 in 1000
F.T.S. para O, white vs. black	0.0047	1.13	258.4 in 1000
F.T.O. para O, white vs. black	0.0968	5.12	1 in 1000
Premature para O, white vs. black	0.0150	0.32	749.0 in 1000
F.T.S. para X, white vs. black	0.0243	4.42	1 in 1000
F.T.O. para X, white vs. black	0.0337	1.32	186.8 in 1000
Premature para X, white vs. black	0.0233	0.53	596.2 in 1000
White para O vs. para X, full term	0.0110	2.08	37.6 in 1000
Black para O vs. para X, full term	0.0274	4.21	1 in 1000
Total cases para O vs. para X, full term	0.0176	4.26	1 in 1000

P.¹=probability of observed difference being due to chance.

in the preceding one which includes premature births, but otherwise the same differences are observed for race, age, and parity as have been previously discussed.

In Table VII, the fetal mortality rates are given according to whether the child is full-term or premature (the latter including all infants weighing between 1500 and 2500 gm. at birth). The full-term labors are divided according as delivery was spontaneous or operative. A study of this table shows that the mortality among premature infants is very high (56.48 per cent), and is considerably increased in the multiparous over the primiparous women. Very little racial difference is here noted, although contrary to the rest of our figures there is a slightly higher mortality among the whites. This finding, however, might be expected when one takes into consideration the fact that the black infant at birth averages between 250 and 300 gm. less than the white.

The difference in the mortality percentage between spontaneous and operative delivery at term is surprisingly high for both races, being about six times as great in the latter group. This would seem to indicate further the benefits of rational conservatism in obstetrics, or earlier interference at a more opportune time in such cases as require operative aid. Attention is again drawn to the higher rate among the multiparae and in the black race.

CONCLUSIONS

1. The gross maternal mortality in a series of 15,370 women delivered after the child has reached the period of viability is 0.79 per cent.
2. Division of the maternal cases according to parity and type of delivery shows that the maternal death rate is consistently higher in the black than in the white race.
3. In this series the mortality rate is higher in multiparae than in primiparae. This is probably due in great part to an abnormal multiparous population.
4. The maternal mortality is lowest following spontaneous delivery at term, increases in the operative type, and is highest when pregnancy terminates prematurely.
5. An increasing mortality is noted in the older age groups, although the girl under seventeen is not an ideal obstetric risk. The optimum age for both races is between seventeen and nineteen years, inclusive.
6. Approximately two-thirds of the maternal deaths are due to infection, toxemia, and hemorrhage. The death rate from infection is almost four times as high in the colored as in the white race. Death from hemorrhage occurs about equally frequently in the two races, while actually more white than black women succumb to toxemia. In our entire series, more deaths resulted from toxemia than from infection.
7. The fetal mortality is significantly higher in the black race; it is also increased in the multiparous women.

8. The fetal death rate increases with advancing age of the mother. The optimum age is seventeen to nineteen years, inclusive, while the results are poorer in the very young woman.

9. Omitting premature infants weighing less than 2500 gm., the still-born and neonatal death rate is 6.33 per cent.

10. The fetal death rate is about six times greater after operative than after spontaneous delivery at term.

THE BROMSULPHALEIN TEST FOR LIVER FUNCTION IN TOXEMIAS OF PREGNANCY

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CLINICAL evidence of renal dysfunction is pronounced in all cases of toxemia of pregnancy, but the phase of liver dysfunction has only recently been investigated, and the interpretation of the results is still far from satisfactory. Phenoltetrabromphthalein-disodium-sulphonate, commercially known as Bromsulphalein, has been estimated to be of value in testing liver function in this variety of toxemia, and previous to the use of this compound, another halogenated phthalein, phenoltetrachlorphthalein, was assumed to have a similar value, according to D'Amory, Krebs and Dieckman, Rosenfeld and Schneider and other investigators. Unfortunately, the intravenous injection of this latter drug caused untoward reactions which discouraged its use, but in 1925, Rosenthal and White discovered the nonirritating properties of bromsulphalein and attention was eventually turned to the use of this dye as a test for liver function in abnormal pregnancy. During the last four years several papers have been published on this subject. To note the general conclusions reached we shall give partial summaries of two of these.

E. S. King, in 1926, by injecting 5 mg. of bromsulphalein per kilogram of body weight and withdrawing a blood sample at the end of one-half an hour, claimed that the percentage of the dye above zero retention, measured colorimetrically, was proportionate to the degree of liver injury present in abnormal cases. There were no data given for normal pregnant women. In the cases of mild toxemia, and in cases where the toxemia was of nephritic origin, the test was negative. In 10 cases of eclampsia, 7 showed dye retention varying from a trace to 40 per cent, and in some cases there was retention on repetition of the test as late as eight days postpartum. All of the patients recovered. Three cases where no retention occurred were classified as "mild eclampsia," "error in technic," and "complicated by chronic nephritis." Three cases of hyperemesis gravidarum showed dye retention varying from 10 to 25 per cent. The degree of retention in all cases was correlated to the severity of the clinical findings.

In 1927, I. A. Siegal, reporting on this same subject, used 2 mg. of bromsulphalein per kilogram of body weight in comparison with King's 5 mg. and withdrew blood samples at the end of a half hour. Their results show wide discrepancies. Siegal's, briefly, were as follows: Sixty-two normal pregnancies showed no

retention of the dye, and eight apparently normal pregnancies showed retention varying from 1 to 3 per cent. Forty-two patients having undifferentiated toxemia manifested by hypertension, albuminuria, and edema showed bromsulphalein retention varying from zero to 5 per cent. Twenty-six patients in this category showed no retention. Six cases of nephritic toxemia had no apparent retention, and, finally, 6 patients with eclampsia eliminated all but amounts from a trace to 3 per cent of the dye. Two patients with hyperemesis gravidarum retained a trace and 1 per cent respectively. The high retentions reported by King were conspicuously absent. Siegal concludes that the test is valuable in diagnosing the degree of toxicity; in differentiating nephritic from preeclamptic toxemia; and in differentiating neurotic from toxic vomiting. He states that perhaps the test is useful as an aid to prognosis in eclamptic cases.

Ordinarily, 2 mg. of bromsulphalein are eliminated entirely in thirty minutes. Because of difficulties in colorimetric reading of this amount, work carried on in the New Haven Hospital in 1926, by Kunkel showed that 5 mg. per kilogram of body weight were removed from the blood in forty-five minutes. No toxic effects followed the injection of this quantity. In the present study, 5 mg. per kilogram of body weight were chosen as standard.

TABLE I. NORMAL PREGNANCY*

CASE	BLOOD PRESSURE	ALBUMINURIA	PER CENT DYE RETENTION AFTER	
			30 MINS.	45 MINS.
1	Normal	0	Trace	0
2	Normal	0	5	0
3	Normal	0	Trace	0
4	Normal	0	Trace	0
5	Normal	0	0	0
6	Normal	0	5	0
7	Normal	0	10	Slight trace
8	Normal	0	Trace	0
9	Normal	0	Trace	0
10	Normal	0	Slight trace	0
11	Normal	0	5	0
12	Normal	0	Trace	0
13	Normal	0	Trace	0
14	Normal	0	Trace	0
15	Normal	0	Trace	0
16	Normal	0	15	Slight trace
17	Normal	0	Trace	0
18	Normal	0	5	Slight trace
19	Normal	0	Trace	0
20	Normal	0	Trace	0

*Slight trace, just appreciable color. Trace, 1 to 4 per cent.

Injections on the calculated basis were given directly into the median antebraclial vein, and blood was withdrawn from the opposite arm into absolutely dry apparatus to prevent hemolysis. By centrifuging after coagulation took place straw colored serum was always obtained. Some of this was alkalinized to bring out the color of the dye and compared with prepared standards and the nonalkalinized serum in a suitable comparator.

In this investigation patients selected for the test were divided into four groups:

1. Twenty women in the last month of normal pregnancy.
2. Seven women with exaggerated vomiting of pregnancy.
3. Thirteen women in whom pregnancy in the last trimester was associated with hypertension, albuminuria, and edema.
4. Eleven women in whom pregnancy in the last trimester was associated with convulsions.

GROUP I. NORMAL CASES. TABLE I

As noted above, each of these normal pregnant women received 5 mg. of bromsulphalein per kilogram of body weight. In the calculation on this basis, the weight of the fetus, amniotic fluid and placenta is included, and thus it is clear that in these cases a quantity of dye actually exceeding 5 mg. per kilo. has been given. However, as can be seen in Table I, the liver normally removes bromsulphalein from the circulation so rapidly that in uncomplicated pregnancy the blood serum contains a barely appreciable quantity of the dye forty-five minutes after its injection. Incidentally, as might be predicted, analysis of the cord blood in two patients who delivered within a half hour after administration of the dye, failed to demonstrate any transfer of the bromsulphalein across the placental barrier.

GROUP II. TABLE II

Of the 7 cases tabulated all but one were in the interval between the first and second trimester and 5 showed no retention of bromsulphalein. One patient in the first trimester entered the hospital following vomiting of five weeks' duration and was notably dehydrated. She began to improve following infusions of saline and glucose but was removed from the clinic before the vomiting had been wholly controlled. Three weeks later, after an interval of no treatment, she was rushed to another hospital where two days after admission she died. At autopsy there were found marked degeneration of the convoluted tubules of the kidneys and degeneration of the central portions of the liver lobules.

The other patient showing retention of bromsulphalein entered the hospital late in the second trimester after having been vomiting for four months. On admission she complained in addition to the vomiting, of urinary frequency and burning and on examination there was tenderness in the right costovertebral angle. Urine examination and cystoscopy revealed a *B. coli* pyelitis on the right, and the vomiting was thought to be a persistent reflex associated with the urinary tract infection. Treatment consisted of urinary antiseptics, the establishment of ureteral drainage by giving large volumes of saline and glucose by infusion and hypodermoclysis. For several days the vomiting was somewhat improved when, within twenty-four hours, the sclerae and skin became intensely jaundiced, and vomiting again increased. The pregnancy was terminated by abdominal hysterotomy. The jaundice disappeared as rapidly as it came and the patient had an uneventful recovery.

GROUP III. TABLE III

In the second group of 13 patients with hypertension, albuminuria, and edema but without convulsions, one gave a history of hypertension and another of edema in a previous pregnancy. A third patient had a previous history of pyelitis and cystitis, and had evidence of urinary infection on admission. In this group, 8 patients showed no retention of the dye. In 5 the test gave a positive result, although in no instance was the retention of the dye greater than 5 per cent. However, the absence of liver dysfunction, as indicated by the results of the test, in no way lessened the severity of the clinical picture. In 9 patients early

TABLE II. EXAGGERATED VOMITING OF PREGNANCY*

NO.	AGE	PARA.	PREV. TOX.	GEST. B.P.	URINE			BLOOD CHEM. N.P.N.	PTHALEIN		RETENTION BROMSUL-PHALEIN	REMARKS		
					ALB.	CASTS	W.B.C.		ACETONE	CULTURE			2 HR. 10 MIN.	RETINAE EDEMA
1	28	i	—	3 mo. 120 80	0	0	Clumps	H.T.	B. coli	25 mg. 60%	Normal	No	0	Recovered
2	24	i	—	2 mo. 80 40	0	0	0	T.	Neg.	24 mg. 55%	Normal	No	0	Recovered
3	29	iii	No	3 mo. 104 70	F.T.	0	0	T.	Neg.	30 mg. 60%	Normal	No	0	Recovered
4	20	i	—	4 mo. 130 70	T.	0	Few	T.	Not taken	31 mg. 55%	Normal	No	0	Recovered
5	23	iv	Pyelitis in 3 mo. 110 3rd. Preg.	60	F.T.	0	0	H.T.	B. coli	38 mg. 55%	Normal	No	10%	Left hospital against advice. Died four weeks later. Autopsy; liver 900 gm. Central lesions.
6	25	iv	No	3 mo. 122 85	F.T.	0	0	T.	Neg.	34 mg. 70%	Normal	No	0	Recovered
7	29	i	—	6 mo. 118 80	0	0	Clumps	T. Bile H.T.	B. coli	26 mg. 65%	Normal	No	20%	Developed icterus. Abdominal hysterotomy. Recovered. Dye retention third day postoperative zero

*H. T., heavy trace. T., trace. F. T., faint trace.

TABLE III. HYPERTENSION, ALBUMINURIA, AND EDEMA WITHOUT CONVULSIONS

NO.	AGE	PARA.	PREV. TOX.	GEST. B.P.	ALB.	CASTS	URINE W.B.C. R.B.C.	CULTURE	BLOOD PITHA- N.P. N. LEIN	RETINAE	EDEMA	BROMSUL- PHALEIN RETENTION	REMARKS
1	23	i	—	8 mo. $\frac{144}{100}$	H.T.	Rare	Clumps	Rare	Staph. A	38 mg. 50%	Sl. edema rt. disc	Gen.	Labor induced. Spontaneous delivery. Recovery uneventful
2	20	ii	Hypertension with First Preg.	9 mo. $\frac{148}{110}$	T.	0	0	0	Neg.	30 mg. 65%	Mod. bilat. edema both discs	Feet and ankles	Labor induced. Spontaneous delivery. Recovery uneventful. Blood pressure on discharge 140/100
3	35	i	—	8 mo. $\frac{160}{100}$	T.	Rare	Clumps	0	B. coli	30 mg. 50%	Early Sclerosis arteries and Edema both discs	Feet	Cesarean section. Uneventful recovery. Liver function test twenty-four hours after operation showed no retention of dye
4	30	iii	No	9 mo. $\frac{210}{130}$	H.T.	Rare	Few	0	Neg.	34 mg. 50%	Albuminuric neuritis	Ankles	Labor induced. Recovery uneventful. Blood pressure on discharge 152/100
5	35	i	—	9 mo. $\frac{154}{100}$	T.	0	0	0	Neg.	26 mg. 60%	Normal	Feet	Spontaneous labor and delivery blood pressure on discharge 130/90
6	35	i	—	7 mo. $\frac{160}{90}$	H.T.	0	Few	0	Not taken	30 mg. 55%	Early sclerosis retinal arteries	Back and feet	Termination of pregnancy. Uneventful recovery. Blood pressure on discharge 120/80
7	21	i	—	8 mo. $\frac{170}{90}$	T.	0	Clumps	0	B. coli	22 mg. 60%	Bilat. edema of discs	General	Labor induced; delivery spontaneous. Recovery. Blood pressure 120/70

TABLE III. (Continued)

NO.	AGE	PARA.	PREV. TOX.	GEST. B. P.	URINE		BLOOD PITHA- N. P. N. LEIN	RETINAE	BROMSUL- PHALEIN		REMARKS			
					ALB.	CASTS			W. B. C.	R. B. C.		EDEMA	RETENTION	
8	39	v	None	8 mo, 160 110	T.	0	Few	0	Not taken	30 mg. 55%	Sclerosis of arte- ries	None	0	Spontaneous premature la- bor. Recovery. Blood pres- sure 130/80
9	39	i	Pyelitis 6 yr. prev.	8 mo, 170 100	H. T.	Few	Num.	0	B. coli	43 mg. 50%	Bilat. edema of discs	General	5%	Elective cesarean section. Recovery. Blood pressure 110/70
10	28	iv	None	7 mo, 180 110	T.	0	Rare	0	Neg.	30 mg. 50%	Normal	None	0	Fetus died in utero. Labor induced. Patient recovered. Blood pressure on dis- charge 130/90
11	38	xiv	None	7 mo, 200 140	H. T.	Few	Few	0	Staph. A.	46 mg. 45%	Hemorrhagic ret- initis	Gen.	Trace	Fetus died in utero. Labor induced. Recovered. Blood pressure 160/90
12	24	iii	Edema 2nd preg.	8 mo, 156 102	H. T.	Num.	Few	0	Staph. A.	22 mg. 50%	Normal	Gen.	0	Labor induced. Spontane- ous delivery. Final blood pressure 130/70
13	21	i	—	9 mo, 160 100	T.	Few	Few	0	B. coli	20 mg. 55%	Normal	Face and Ankles	0	Spontaneous labor and re- covery

TABLE IV. TOXEMIA WITH CONVULSIONS

NO.	AGE	PARA.	PREV. TOX.	GEST. B.P.	URINE				BLOOD N.P.N.	PHTHALEIN	RETINAE	BROMSULPHALEIN REACTION		REMARKS
					ALB. GM./L.	CASTS	W.B.C.	R.B.C.				EDEMA	TENTION	
1	35	iv	None	8 mo. $\frac{170}{110}$	14	Num.	Few	0	B. coli	32 mg.	55%	Bilat. edema of discs	Back and feet 15%	Two convulsions. Labor induced. Spontaneous delivery dead fetus. Hem. Staph. infection—died 14 days post-partum
2	29	i	—	7 mo. $\frac{180}{100}$	5	Few	Few	0	Neg.	29 mg.	40%	Edema discs and early sclerosis of arteries	General 15%	Two convulsions. Pulmonary edema and cardiac collapse. Died undelivered three days after admission.
3	32	v	Convulsions second and third pregnancies	1 day 148 p. p. $\frac{90}{90}$	7	Few	Few	0	Not taken	70 mg.	Not obtained	Edema both discs	General 15%	Several convulsions followed by death three days post-partum
4	32	i	Preexisting hypertension and nephritis	7 mo. $\frac{170}{120}$	1	0	Few	0	Neg.	37 mg.	30%	Bilat. optic neuritis and retinitis	None 5%	One convulsion. Elective section and premature delivery. Recovery uneventful. Blood pressure on discharge 140/90
5	43	vi	11 year interval between pregnancies	8 mo. $\frac{180}{110}$	4	Few	Num.	0	B. coli	39 mg.	35%	Edema discs. Detached retina on right	General 0	Four short convulsions. Spontaneous onset of labor; instrumental delivery. Normal puerperium.
6	22	i	—	9 mo. $\frac{152}{100}$	1	Few	Few	0	Neg.	32 mg.	60%	Not examined	Feet Trace	Labor induced. Three convulsions during first stage. Instrumental delivery. Puerperium febrile causes?

TABLE IV (Continued)

NO.	AGE	PARA.	PREV. TOX.	GEST. B.P.	URINE			BLOOD N. P. N.	PHTHA- LEIN	RETINAE	BROMSUL- PHALEIN RE- EDEMA TENTION		REMARKS
					ALB. GM./L.	CASTS	W. B. C.	R. B. C.	CULTURE				
7	19	i	—	7 mo. $\frac{190}{120}$	7.5	Num.	Few	0	B. coli	40 mg.	Not satis- factory	Edema of discs Ankles 20%	Three convulsions. Labor in- duced and spontaneous de- livery of dead fetus. Re- covery uneventful. Final blood pressure 120/80
8	30	i	—	9 mo. $\frac{168}{100}$	1.5	Num.	Few	0	S. aureus	25 mg.	70%	Bilat. edema of discs and retinal hemorrhages	One convulsion. Labor in- duced and delivery by ver- sion. Fetus normal. Recovery uneventful. Blood pressure 130/70
9	32	viii	None	8 mo. $\frac{180}{110}$	5	Few	Few	0	S. aureus	35 mg.	Not satis- factory	Edema of discs Feet 0	Six convulsions. Labor in- duced. Spontaneous delivery and good recovery. Final blood pressure 190/130—18 days postpartum
10	24	ii	None	8 mo. $\frac{145}{110}$	10	Num.	Few	0	S. aureus	32 mg.	55%	Edema of discs Face hands and feet 5%	In labor. Three convulsions and instrumental delivery. Rapid recovery. Discharge blood pressure 120/80
11	15	i	—	8 mo. $\frac{155}{110}$	9	Num.	Few	0	Nonhem. S.	31 mg.	Oli- guria and detached lt. retina	Edema of discs Gen. 0	Six convulsions. Labor in- duced and macerated fetus delivered. Slow recovery. Final blood pressure 120/80

sclerotic or albuminuric retinal changes were present as diagnosed by Dr. Eugene Blake of New Haven. In the majority of the group the pregnancy was terminated artificially.

GROUP IV. TABLE IV

Of the 11 patients whose pregnancy was associated with convulsions, one gave a history of a preexisting hypertension and chronic nephritis; a second patient pregnant for the fifth time had convulsions during the second and third pregnancies; and in a third patient the interval between the present and previous pregnancy was eleven years. In this group 5 patients showed no retention of the dye; one showed a trace. Of the remaining, 3 showed a retention of 15 per cent and died, one of infection, and 2 of toxemia. One patient in whom the retention was 20 per cent recovered following the induction of labor and the expulsion of a dead fetus.

SUMMARY

The findings in the tables may be summarized as follows: Of 20 normally pregnant women in the last month of pregnancy, there were 3 whose serum showed a trace of bromsulphalein forty-five minutes after its injection. Of the seven women in the first or second trimester with exaggerated vomiting, two showed marked retention of the dye, the others none. One with retention left the service against advice and died four weeks later in another hospital, the other developed acute jaundice and recovered after termination of the pregnancy. In the group composed of 13 women with hypertension, albuminuria and edema unassociated with convulsions, the retention of the dye was in no instance greater than 5 per cent. However, in these patients the clinical picture, in spite of the absence of liver dysfunction, was grave. In 9, sclerotic or albuminuric retinal changes were present, and in the majority pregnancy was artificially terminated. In the last group where pregnancy was associated in the last trimester with toxemia and convulsions, 5 showed not more than a trace of retention. Three in whom the retention was 15 per cent died, one from postpartum infection, and the others from the toxemia antepartum. In contrast the patient, who of the entire group showed the highest percentage of retention, 20 per cent, recovered following the induction of labor.

COMMENT

In interpreting the results of this investigation, it is essential that we remember that the retention of bromsulphalein indicates only a degree of impaired liver function and not actual liver pathology. The question arises as to how much the liver must be damaged before that injury can be shown by functional tests. This question has been somewhat answered by the results of animal experimentations. Rosenthal found that 12 per cent of the liver of rabbits must be removed before variations in the excretion of phenoltetrachlorophthalein can be detected, and Rous and McMaster found that one-fourth of the liver in rats will maintain normal function. Undoubtedly there are great variations in the amount of damage that will impair function, and how much of

the human liver will support normal function is unknown. We do know, however, that all organs functionally have a large factor of safety, and thus while a negative test for liver function does not indicate that pathologic changes are absent, a positive case does indicate that the safety limit for the functioning of that organ is exceeded. What alteration of function over the safety limit would be fatal to the individual is also unknown, but Baronberg, in studying liver function in acute infectious diseases, frequently found alterations in liver function in the acute stages of pneumonia that were comparable to those encountered in inflammatory and degenerative hepatopathies; and in these cases, function again became normal with recovery from the disease.

It is noticeable in the present investigation that in toxemias late in pregnancy liver dysfunction even in fatal cases did not exceed 15 per cent, except in one instance where it was 20 per cent and that patient recovered. Moreover, those cases which showed any retention above a trace could not be considered more critically ill from a clinical viewpoint than most of the others who showed no evidence of liver dysfunction. It, therefore, seems improbable that the gravity of the situation in cases late in pregnancy can be pronounced proportional to such relatively small degrees of liver dysfunction. Of more significance, however, are the evidences of liver dysfunction early in pregnancy. Here where there is a question between an uncontrolled reflex phenomenon or the establishment of a vicious cycle of vomiting which has gradually brought about organic changes, retention of bromsulphalein can be regarded as an aid to diagnosis, and probably to estimate response to treatment. Nevertheless, it is our opinion that, from the clinical picture alone in such cases, one cannot defer treatment too long on the basis of this single observation.

CONCLUSIONS

In this small number of cases we feel the following facts have been established:

1. In normal pregnant women, the blood serum showed at most a barely appreciable retention of bromsulphalein forty-five minutes after the injection of the dye in amount somewhat in excess of 5 mg. per kilo.
2. The serum of women whose pregnancy was early associated with exaggerated vomiting showed marked retention of the dye in two cases which could be said to have gone on to a toxic state, although the factor of infection must be considered in one of these.
3. Of 13 women whose pregnancy was associated in the last trimester with hypertension, albuminuria and edema, 2 showed a retention in the serum of 5 per cent; 11 had a retention of zero or but a trace.
4. In 11 women whose pregnancy was complicated in the last trimester with toxemia and convulsions, there was in 4 no retention of the dye, and in one but a trace. In the 3 whose serum showed a retention of 15 per cent, one died of a postpartum infection and the others of

the toxemia antepartum. In contrast, an additional patient whose serum retained 20 per cent of the dye, the highest percentage in the entire group, recovered following the artificial termination of the pregnancy.

5. From a study of this group of cases, we find the bromsulphalein test of value in determining the degree of toxicity in exaggerated vomiting cases in early pregnancy; but we are unable to convince ourselves of its value late in pregnancy either as a means for differentiating the nephritic from the eclamptic toxemia or as an aid in predicting the outcome in these conditions.

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15 STATE STREET

CALCIUM AND INORGANIC PHOSPHORUS CONTENT OF PRENATAL AND POSTPARTUM SERUM

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EVER since the development of modern methods of chemical blood analysis, the significance of the variations of the calcium and inorganic phosphorus of the serum, especially during pregnancy, has been the subject of interest and study.

Although Morley¹ in 1913, using the method and arbitrary standard of Bell² reported a lowering of serum calcium during pregnancy, labor, and puerperium, most of the early workers were agreed that the calcium concentrations remained within the limits of the accepted normal range of 9 to 11 mg. of calcium per 100 c.c. of serum.

In 1923, Widdows³ introduced the innovation of following individual cases over an extended period. By this method she reached the conclusion that there was a tendency, first, to a decrease in the calcium content of the blood in late pregnancy, which was not manifest in all cases, and later, to a rise directly after confinement, even during lactation. The results of this work also called into question the validity of the accepted normal range of serum calcium.

Denis and King⁴ reported that the serum calcium in 64 cases of normal pregnancy ranged between 10.2 and 11.9 mg., averaging 10.8 mg. Since this series included cases from the second to the ninth month, it would seem to indicate that the calcium concentration does not fall even during the latter months of gestation. No attempt was made, however, to determine individual variation; the series

was composed of single determinations on 64 cases. Handelman, Rose, and Sherwin⁵ supported this view, finding calcium concentrations normal during gestation with 11.3 mg. average for the sixth, seventh, eighth, and ninth months. They found a slight decrease immediately after parturition, but a rise to a high normal before dismissal. They made repeated observations but used only 10 cases, less than half of which had a complete series of determinations. Their conclusions, therefore, cannot be accepted as final.

Serdyukov and Morosova⁶ likewise failed to find any change in calcium concentration during pregnancy. They found a rather high normal, 9.0 to 13.7 mg., average 11.25 mg., for 45 cases, and little variation from this range during the first half of pregnancy, the latter half, or childbirth, although the average during childbirth (7 cases) was slightly lower than for the first or second half of pregnancy (19 and 50 cases respectively). In cord blood, however, the concentration ran definitely higher.

In opposition to these views, Stieglitz⁷ found a mild hypocalcemia during the last months of pregnancy, a rise after delivery, and a transient fall in calcium at the onset of lactation. Quoting Wyss⁸ and Anderson⁹ for his standards, he found that practically all of his determinations fell within the normal range: 88 per cent were between 9 and 13 mg. and 60 per cent between 10 and 12 mg. Bokelmann and Bock¹⁰ also reported a slight decrease in total calcium of the serum during pregnancy, but they found it relatively high, an actual increase, at the onset of delivery, although it fell again to the low level of the latter half of the pregnancy by the end of the delivery.

Cantarow, Montgomery and Bolton¹¹ summed up the recent literature with the conclusion that total serum calcium diminishes during the latter months of pregnancy, but is usually above the lower normal limit. They attributed symptoms to variations in the distribution of diffusible and nondiffusible forms. Damble¹² agreed that there is a fall. Using 10 cases he found 9.36 mg. for the second half of pregnancy, 9.75 immediately after delivery, and 9.82 on the fifth day postpartum. He gave 9.97 mg. as normal. Harding, Murphy, and Downs¹³ were in close agreement with his postpartum figures. They found 9.7 mg. the average of 136 cases on the tenth day, with a range of 8 to 12 mg.

Hellmuth and Timpe¹⁴ also found that there was a fall in calcium, but their figures were quite different. They gave 10.5 mg. per cent as the average for the nonpregnant normal (range 8.5 to 11.6 mg. in 23 cases), 10.2 mg. for the first, and 9.5 mg. for the latter half of pregnancy, rising to 10.2 mg. in puerperium. They did not find the dializable portion altered.

From this brief survey it is apparent that there still exists a wide diversity of opinion as to what changes in the serum calcium content, if any, actually occur during pregnancy. It is also apparent that the question hinges on what may be considered the normal range of variation. The figures already quoted show that investigators may be divided roughly into two groups, one of which holds that the heretofore accepted range of 9 to 11 mg. is normal for nonpregnant normal women, the other claiming that a higher range is more nearly correct.

Spiegler and Schol¹⁵ assumed the normal average to be about 10.6 mg. on the basis of results quoted from the literature. These included Jansen who gives 9.4 to 11.0, average 10.2 mg.; v. Oettingen average 10.2 mg.; Schoning 10.5 to 11.5 mg.; Kylin 10.6 to 12 mg.; and Rodecrest average 11.97 mg. The 155 determinations they made covering the course of pregnancy from the third month until after delivery were all above 10.0 mg., according to their Curve I.

Bock, on the other hand, found the normal average to run much lower. In a series of articles, Bock^{16, 17, 18} gave normal calcium figures as 9.6 mg., 9.6 to 9.9 mg. (3 cases), and 9.65 mg. (average of 12 cases). Bokelmann and Bock¹⁹ raised these figures to 10.1 mg. per cent for the normal calcium content of blood. Even with such low normal ranges they did find some slight lowering of the calcium concentrations during the latter months of pregnancy, but the variations were so slight, that with the small number of cases reported, some natural doubt arises as to their accuracy.

Higher normal ranges are more frequent. Kylin²⁰ gave 10.6 to 12 mg. with an average of 11.13 mg. For those below twenty-one years of age the average was slightly higher, while above 41 it was somewhat lower. Brems²¹ had a similar range, 10.48 to 13.86, average 11.48 mg. (23 cases). Allen and Goldthorpe²² using the Tweedy process found 19 nurses to come between 9.3 and 13.6 mg. calcium per 100 c.c. of plasma, while Cantarow, Dodek, and Gordon²³ gave 10.09 to 10.45 mg. as normal (6 cases). This is in accord with the figures of Halverson, Mohler, and Bergeim²⁴ for women.

In an attempt to settle this question Rosen and Krasnow²⁵ made a study of 50 medical students, using the Kramer-Tisdall method. They found a range of 10.7 to 13.2 mg., average 11.6 mg. Roe and Kahn²⁶ repeated this work, also using 50 medical students, but making the determinations by their colorimetric method. They found the range to be 9.0 to 11.6, average 10.13 mg. With 46 per cent of the cases falling between 9.0 and 9.9, this seems in complete accord with the old normal range.

In regard to the calcium concentration in the umbilical cord blood, there is entire agreement. Serdyukov and Morosova,⁶ Bokelmann and Bock¹⁷ and Hellmuth²⁸ all found the fetal concentration definitely higher than the maternal, the first named to the extent of about 20 per cent.

Bock²⁰ found no noticeable change from the normal in the inorganic phosphorus averages during pregnancy, though individual variations are large. He did find a fall, about 10 per cent, postpartum, which returned to normal within a week.

As to calcium and phosphorus metabolism, most investigators seem to agree that there is an unfavorable or negative balance at least during the latter part of pregnancy, and often lasting through lactation. This may be relieved to some extent by additions to the diet.

Observations we have made in our study of the problem favor the higher figures, and, while they do not clear up the problem are of value in that they add to the sum of our knowledge by which the final solution may be reached.

METHOD

Our subjects were dispensary patients, chosen at random. No effort was made to regulate their diets, beyond the usual clinical advice as to milk, fruit, and vegetables. Table I covers a study of such cases during their stay in the hospital. Table II includes only data from patients living at home, with the exception of the figures in column 3. Cases delivered in the hospital (figures in column 3) were discharged at twelve to fourteen days. Table III gives data from home cases coming into the dispensary.

Calcium determinations were made by a modified Kramer and Tisdall³⁰ method. Two cubic centimeters of fresh serum were precipitated with ammonium oxalate

and allowed to stand eighteen to twenty hours. The precipitate was washed, dissolved in normal sulphuric acid, and titrated against freshly diluted and standardized potassium permanganate. This daily standardization of the permanganate also provided an end point for each series of determinations, eliminating the variations due to alteration of the light on different days. Checks on the calcium determinations have been made at intervals during the course of study against known standards; by recovery of calcium added to samples of serum; and by multiple determinations on the same serum. These tests indicate an average error of about one per cent. In view of this, and of the uniformity observed in our determinations, we feel justified in attaching significance to alterations amounting to three per cent or more.

We have made our phosphorus determinations according to the method of Kuttner and Cohen as modified by Kuttner and Liechtenstein²³ observing certain precautions suggested by Doctor Shohl's laboratory. These included using five standards instead of two, equal to 2.5, 3.75, 5.0, 7.5 and 10 mg. P per 100 c.c. of serum, which permitted all colorimeter readings to be made within 3 mm., plus or minus, of the standard, set at 20 mm. They also included constant stirring during the addition of the stannous chloride; completion of said addition for the entire run in ten minutes with the standards in the middle; twenty minutes aging before reading; and completion of readings in two hours.

The method as employed by us has been tested in the way mentioned above and has been found to have an accuracy of about 6 per cent. Two cubic centimeters of the serum, removed from the clot in from one-half to one hour and a half after drawing, give duplicate tests. Hemolized samples were discarded. The figures given for both calcium and phosphorus are the average of duplicate determinations.

DISCUSSION OF RESULTS

It is at once apparent from a study of Table I that the calcium and inorganic phosphorus in the serum of the fetal blood, as taken from the umbilical cord, is higher than that of the mother. As regards calcium, the values of the cord blood are in every case higher than those of the corresponding maternal blood throughout the entire series. The phosphorus shows but two exceptions, one of which is equal and one higher. Since this finding is in accord with that of previous observers, it may be regarded as a fact in normal cases.

It is also apparent that there is little variation in venous serum calcium among the average values obtained before delivery, at delivery, and two days after delivery. This is substantiated by the additional cases given at the foot of the table. This would indicate that neither the actual exertion of delivery nor the anesthetic has any particular effect on the calcium content of the blood. The phosphorus variations are greater both in the averages and individually, but it would appear that there is an increase at delivery, followed by a fall two days later, and a subsequent rise at seven days postpartum. In the additional cases the average of the few cases shown give at delivery higher venous values than cord; but, since there are so few of these, and they are not from corresponding cases, this fact cannot be regarded as very significant.

Of equal interest is the fact that the calcium values, on the basis of the old normal range, are so high. At the onset of labor the averages given

TABLE I. VARIATIONS BETWEEN MATERNAL AND FETAL SERUM CA AND P.
ALL FIGURES ARE GIVEN IN MG. PER 100 C.C. OF SERUM

CASE	ONSET OF LABOR			DELIVERY				POSTPARTUM				AGE	PARA
	VENOUS BLOOD		HOURS BEFORE DELIVERY	CORD BLOOD		VENOUS BLOOD		SECOND DAY		SEVENTH DAY			
	CA	P	CA	P	CA	P	CA	P	CA	P			
1	9.8	3.7	3	10.8	5.1	9.3	4.0	9.5	3.9	9.8	4.4	20	i
2	9.7	5.4	5	11.0	7.3	9.6	5.8	9.6	4.1	9.5	5.0	20	i
3	9.2	4.2	4	11.0	6.5	9.1	2.9	9.6	4.0	9.8	3.9	30	v
4	9.5	3.3	3	12.6	5.2	10.2	3.7	10.4	3.7	10.5	4.3	17	i
5	9.2	2.7	3.5	11.5	5.5	9.3	3.7	10.0	3.9	10.3	4.1	30	iii
6	9.6	4.0	5	11.1	6.1	9.8	5.1	9.6	3.6	10.3	4.6	18	ii
7	9.2	3.5	11	11.6	7.6	9.2	6.5	9.4	4.0	9.9	3.8	26	i
8	9.8	3.9	6	10.9	7.1	10.0	5.4	9.5	3.5	9.9	4.7	19	i
9	10.2	4.9	16	11.9	6.3	9.9	5.5	9.8	3.6	10.4	3.8	19	i
10	9.6	3.0	3	13.1	6.5	9.8	4.1	11.0	3.8	10.2	4.2	20	i
11	9.3	3.5	2	12.9		9.6	3.8	9.8	ppt.	10.2	3.8	21	i
12	9.9	3.6	5.5	11.6	3.8	9.9	3.7	10.2	3.8	10.1	4.6	23	i
13	9.6	3.8	7.5	12.0	7.2	9.9	5.1	9.3	3.4	10.1	3.8	23	i
14	9.5	3.9	8	11.9	5.7	10.4	5.0	10.0	3.2	10.7	4.6	32	i
15	10.0	4.1	7	11.9	7.1	10.0	6.1	10.0	4.0	10.1	4.0	17	i
16	9.1	3.6	2.5	10.2	5.6	9.1	4.6	8.9	3.6	9.3	4.1	31	vi
17	10.2	3.6	7	12.5	5.6	10.3	5.2	10.2	3.8	9.7	4.1	20	i
18	9.6	3.4	3.5	11.1	5.4	10.0	3.8	9.9	3.7	10.5	ppt.	26	i
19	10.2	3.9	7	11.7	5.9	10.1	4.4	10.4	4.7	10.9	4.9	28	ii
20	10.2	2.5	7	11.2	4.8	9.9	3.7	9.3	2.3	10.6	4.1	19	i
AV.	9.7	3.7	5.8	11.6	6.0	9.8	4.6	9.8	3.7	10.1	4.3	23	
Additional cases of incomplete series													
NO. OF CASES	24	20		16	15	10	9	15	12	21	19		
AVER-AGE	10.0	3.6		11.8	5.6	10.2	6.3	10.1	3.9	10.5	3.8		

are 9.7 mg. and 10.0 mg. per 100 c.c. of blood, with 9.1 mg. the lowest for the entire forty-four. The average delivery figures are almost identical with these, as are also those of the second day postpartum, shading up if anything. The seventh day shows a definite rise. In the whole table, including the additions at the bottom, there is only one value below 9.0, and that, 8.9 mg., was from the mother of twins on the second day postpartum.

These figures are substantiated by the values given in Table II, where again there is only one determination below 9.0, also 8.9 mg. The averages of 9.9 mg. for six weeks and two weeks before delivery fit in well with the onset of labor values of Table I, and indicate one of two things; either that calcium does not fall during the latter part of pregnancy; or, that the supposed normal range of 9.0 to 11.0 is too low. If the latter supposition is true, it explains the failure of many investigators to observe a fall in serum calcium during pregnancy. The postpartum figures might be taken as an indication favoring this latter view, with averages

of 10.5 mg. and 10.4 mg. respectively. It is worth noting that after six weeks 31 cases, most of which were nursing, gave only four figures below 10.0 mg. the lowest being 9.5 mg.

The 21 additional cases presented in Table III give the same average as those in Table II, 10.4 mg. per 100 c.c. for six weeks postpartum. Here 4 of the 5 cases where the baby was not being nursed by the mother fall below the average figure, while the 4 shown at seven, eight, and twelve weeks all equal or surpass it. The range here is also high, with only 4 cases below 10.0 mg., the lowest being 9.4 mg. Tests conducted on 60 normal, nonpregnant young women are in entire accord, averaging 10.4 mg., with 9.3 the lowest of the five values found below 10 mg.

The phosphorus averages of Table II fit in well with those of Table I. The predelivery figures are a little lower than those at onset of labor, but

TABLE II. SERUM CALCIUM AND INORGANIC PHOSPHORUS BEFORE AND AFTER DELIVERY

ALL FIGURES ARE GIVEN IN MG. PER 100 C.C. OF SERUM

CASE	BEFORE DELIVERY				POSTPARTUM				REMARKS
	6 WEEKS		2 WEEKS		12-14 DAYS		6 WEEKS		
	CA	P	CA	P	CA	P	CA	P	
45	9.3	2.5			10.9	4.1	10.9	3.6	Nursing Sup. feeding (7 wk.)
46	10.5	3.6	11.0	3.4			10.3		
47	10.6	3.6					10.5	3.2	
48	9.8	3.5			10.5	4.0	10.0	3.9	
49	10.7	2.9	9.9	3.5	11.5	4.1	10.6	3.7	Nursing
50			10.0	3.8	10.8	4.0	11.1	4.3	Nursing
51	10.0	3.0					10.2	3.4	Nursing
52	9.8	3.4			10.4	4.1	10.2	2.8	
53	9.6		9.1	3.4			11.1	3.9	Nursing
54	9.7	2.5	10.5	2.7	10.0	3.4	9.9	2.7	Nursing
55	9.5	3.3					9.9		Nursing
56			8.9	3.5	11.9	4.4	10.4	5.1	Nursing
57	10.0	2.9					10.3	3.5	Baby stillborn
58			9.5	3.5			10.3	3.6	Nursing (7 wk.)
59	9.8	3.1	10.2	3.0	10.0	5.1	10.4	4.0	Not nursing
60			10.2	2.8	10.2	4.2	10.8	4.4	Nursing
61	10.3	2.9					10.5	3.8	Nursing
62					10.0	5.2	10.4	3.7	Nursing
63	9.3	4.0	9.5	3.8			10.4	4.4	Nursing
64	11.0	3.4					10.6	3.7	Nursing
65	10.1	4.3	9.9	4.0			10.3	3.5	Nursing
66			9.7	2.9	10.3	6.3	10.6	3.9	Nursing
67	9.6	3.2	10.2	3.6	10.9	3.9	10.2	5.0	Nursing
68	9.9	2.9	9.0	2.7	10.0	4.5	9.8	4.8	Nursing
69			10.0	3.4	11.6	4.2	10.4	3.6	Nursing
70	9.3	2.9					10.0	3.7	Nursing
71	9.4	3.1	10.2	2.5	9.7	3.8	10.2	4.1	Nursing
72	9.5	3.8	9.4	4.1	9.6	5.1	9.5	4.3	Nursing
73	10.8	3.6	10.3	3.0			10.5	3.4	Nursing (4 wk.)
74	10.1	2.6	11.0	3.5	10.6	4.2	11.0	3.6	Sup. feeding
75	9.8	3.2	9.0	2.7	10.0	4.1	10.0	4.2	Nursing
AV.	9.9	3.2	9.9	3.3	10.5	4.4	10.4	3.9	

the 4.4 mg. found two weeks postpartum is very close to the averages of 4.3 and 3.8 mg. for seven days, while the 3.9 and 3.8 mg. averages of Tables II and III at six weeks may be considered as the same. Individual variations are greater than with calcium, but on the whole the indications are that there is a high point at the time of delivery, followed by a fall of short duration, then a gradual rise to a level slightly higher than that of the latter part of the pregnancy.

TABLE III. POSTPARTUM SERUM CALCIUM AND INORGANIC PHOSPHORUS
ALL FIGURES ARE GIVEN IN MG. PER 100 C.C. OF SERUM

CASE	WEEKS POSTPARTUM	CA.	P	REMARKS
76	6	10.7	4.2	
77	7	11.2	4.1	Nursing
78	6	10.3	3.5	Nursing
79	6	9.8		Nursing
80	12	10.4	2.9	Nursing
81	6	10.7	4.4	Nursing
82	6	10.6	3.5	Nursing
83	8	10.5	3.5	Nursing
84	8	10.6	3.8	Nursing
85	6	10.7	2.7	Nursing
86	6	10.0	4.4	Baby died at 7 days
87	6	11.1	3.8	Nursing
88	6	9.9	3.5	Not nursing
89	6	9.4	3.4	Nursing
90	6	10.5	4.1	Stillborn baby
91	6	9.9	3.5	Not nursing
92	6	11.3	4.8	Nursing
93	4	10.3	3.8	Not nursing
94	6	10.0	4.0	Nursing
95	6	10.6	4.1	Nursing
96	6	10.2	4.2	Nursing
AV.		10.4	3.8	

SUMMARY

Data presented show that the serum of the fetus, as sampled from the umbilical cord, is higher in calcium and inorganic phosphorus than that of the mother at the time of delivery. This is in accord with the observations of previous investigators. In 36 cases the cord serum averages 11.7 mg. calcium. The average for the mother in 44 cases is found to be 9.8 mg. of calcium per 100 c.c. of serum at onset of labor, and no significant change is found at delivery or two days postpartum. The averages, however, for the seventh day postpartum, 10.3 mg. for 41 cases, and for the twelfth to fourteenth day, 10.5 mg. for 18 cases, indicate a gradual rise in calcium following delivery. At six weeks or more postpartum, 10.4 mg. per 100 c.c. was found to be the average of 52 cases, most of whom were nursing. Only eight were below 10.0 mg., the lowest being 9.4 mg. Since 10.4 mg. was also the average found for 60 normal

women it is suggested that the lower limit of the accepted normal range, 9.0 mg. per 100 c.c. may be too low.

The inorganic phosphorus averages indicate a slight rise during the latter stages of pregnancy, reaching a peak at delivery, 5.1 mg. in 35 cases, followed by a short decline, and a subsequent recovery to a little higher than the predelivery level. Three and seven-tenths mg. to 3.9 mg. was found to be the phosphorus average of the mothers, most of whom were nursing, at six weeks postpartum. The cord blood averaged 5.8 mg. inorganic phosphorus in 36 cases.

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2105 ADELBERT ROAD

Anselmino, K., and Hoffman, F.: Antiglycogen Substance (Thyroid Hormone) in the Blood of Pregnant Women. Arch. f. Gynäk. 143: 310, 1930.

The authors demonstrated a substance in the blood of pregnant women which has the power of decreasing the glycogen content of the liver of a mouse. This substance is present in the blood after the second month of pregnancy and gradually increases in amount throughout pregnancy. It is at its maximum concentration at the onset of labor, begins to decrease on the second day postpartum and has disappeared after the eighth day postpartum. It is present in the fetal blood stream as well but in much smaller amounts than are found in the maternal blood. This substance is identified as a thyroid gland hormone. Two and a half c.c. of blood from a pregnant woman will produce a decrease in the glycogen content of the mouse liver up to 75 per cent. This corresponds to the action of 40 to 50 units of thyroxin.

RALPH A. REIS.

COAGULABILITY OF THE BLOOD IN PREGNANCY

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AT THE present time there prevail opposing views regarding the coagulability of the blood in pregnancy and in the puerperium. This disagreement is brought about mainly by the fact that the simple determination of the coagulation time, the test usually employed as an index of the coagulability of the blood, is surrounded by inherent difficulties. The multiplicity of methods devised for the determination

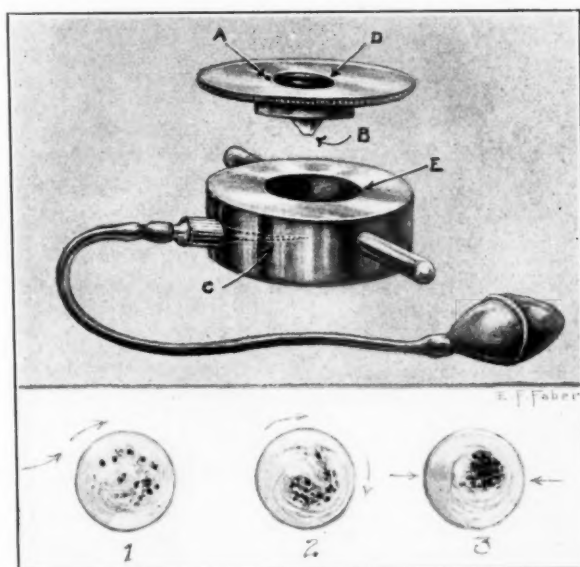


Fig. 1.—Bogg's coagulometer employed in determination of coagulation time. A, air vent allowing an equalization of pressure in the chamber (E) when air is blown in. B, glass cone. C, metal tube projecting into chamber. D, glass window.

of clotting time, and the variant results obtained by these methods, point to the uncertainty of the test in gauging the coagulating property of the blood. For this reason, it is practically impossible to satisfactorily compare and evaluate results reported by numerous observers for both normal and pathologic conditions.

The present study was conducted to determine the blood coagulation time in pregnancy and in the lying-in period, with the purpose to ascertain if this test could be depended upon to render reliable information regarding the coagulability of the blood. The instrument employed in this investigation was selected with especial care because of the shortcomings of some of the methods offered for the test. A method both accurate and simple in technic was desirable. For this reason the

Bogg's modification of the Brodie-Russell's instrument was chosen (Fig. 1), with the realization, however, that an infallible method has yet to be developed. One qualified technician performed all the tests in order to minimize as much as possible the error due to personal equation, which is claimed by Solis Cohen to be important in this method.

The literature on the subject leads to the conclusion that there is great difference of opinion concerning the degree of ability of the blood to coagulate in pregnancy. Several authors (Cohen, Hartman, Cristea) claim that the coagulability is unchanged in pregnancy, while numerous others have reported that there is a discernible shortening of the coagulation time during gestation, immediately after labor, and in the beginning of the puerperium.

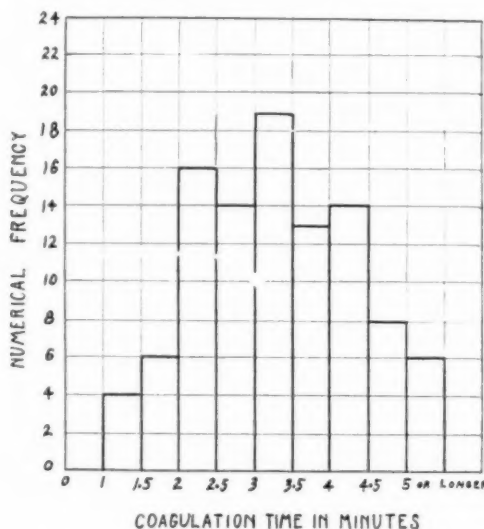


Fig. 2.—Histogram of grouped numerical frequencies of coagulation time in tests on 100 normal nonpregnant women.

In general, most of them report a shortening of the coagulation time in pregnancy, which returns to normal at the end of the puerperium.

TECHNIC

In the determination of the coagulation time by means of the Bogg's coagulometer, the progress of coagulation is directly observed in a drop of blood contained in a suitable moist chamber and set in rotation by a very fine stream of air tangentially directed at it. The coagulometer consists of a chamber (E, Fig. 1) into which a glass cone projects from above (B), terminating in a surface of 4 mm. in diameter. A metal tube (C) projects into the chamber from the side and ends in a tip close to the lower surface of the cone.

The test is performed as follows:

The cone (B) is touched at right angles to a large drop of blood from a free flowing puncture and not dipped into it. The time is noted with a stop watch. The cone is then promptly adjusted in the chamber, the instrument quickly placed upon

the stage of the microscope and the drop of blood is observed under the low power. A gentle blast of air is turned against the edge of the drop every thirty seconds by squeezing the bulb. This causes a rapid circular movement of the erythrocytes (1 and 2, Fig. 1). As soon as fibrin formation takes place, the independent movement of the single corpuscles ceases and they begin to move in larger masses. The progress of coagulation is tested from time to time with gentle currents of air until the radial elastic motion is observed, as of a rubber ball pressed in at one point. The coagulation time is counted from the moment the blood appears at the surface of the wound until this end-point is reached. Absolute cleanliness of the apparatus is essential to secure accurate results. Pressure upon the tissues or congestion of the part punctured will increase the coagulability of the blood and must be avoided.

The coagulation time of the blood was determined in 400 women registering at the antenatal clinic of the Jefferson Medical College Hospital, at various intervals in pregnancy. In 100 of these patients, additional tests were performed twenty-four to forty-eight hours after completion of labor, three to five days after delivery, and between the eighth and tenth day of the puerperium. To properly evaluate the results obtained in pregnancy, the clotting time was also estimated for 100 normal young nonpregnant women (Fig. 2). The shortest time observed was one minute, while the longest was seven minutes. It is readily noted that the coagulation time readings tend to center in duration somewhere in the neighborhood of two and five-tenths to four minutes inclusive (62 per cent). Only 36 per cent of the normal individuals gave clotting times, ranging between one and five-tenths and two and five-tenths minutes, while in 60 individuals (60 per cent) the clotting time was prolonged beyond two and five-tenths minutes. These results are in accord with those reported by Murphy and Gould, for the normal individual, who used the same type of coagulometer.

In recording the results of the test throughout this study, the following unalterable rule was followed:

A coagulation time with a fraction of a minute less than fifteen seconds was recorded with the time of the immediate lower figure. Accordingly, a coagulation reading of two minutes and twelve seconds was recorded as being two minutes, whereas a clotting time of two minutes and twenty-two seconds was listed as two and five-tenths minutes. Although differences in coagulation time of fifteen to thirty seconds are insignificant where there is a large time range for normal readings, it was believed that the results could be more satisfactorily and accurately compared if such minute changes were recorded.

It might be interesting here briefly to summarize (Table I) the various normal readings of coagulation time obtained and reported by different observers. From an analysis of these results one may be justified in concluding that an absolute normal clotting time does not exist. For a detailed description of the many methods and coagulometers devised for the estimation of the coagulating time, the reader is referred to the communication by Solis Cohen, from whose conclusive study the above figures have been abstracted.

TABLE I. NORMAL COAGULATION TIME OBTAINED WITH DIFFERENT METHODS

METHOD	TIME IN MINUTES
Vierodt's	9.5
Wright's	2.5 to 5
McGowan's	8
Addis' Modification of McGowan's	9.5
Brodie-Russell's	3 to 8
Bogg's Modification of Brodie-Russell's	3 to 8
Addis' Modification of Brodie-Russell's	8
Cohen's Modification of Milian's	8.66
Milian's	15 to 34
Morawitz's	5
Sabrazes'	9 to 10

OBSERVATIONS IN PREGNANCY

The test was performed on 49 women during the first four months of gestation, on 98 in the fifth and six months, on 187 in the seventh or eighth month, and on 66 in the last month. Of the 49 tests performed in the first four months of gestation, 33 or 67.3 per cent gave a coagulation time of one and five-tenths to two and five-tenths minutes (both figures are inclusive). A coagulation time of one and five-tenths to two and five-tenths minutes was also obtained in the other periods of pregnancy as follows: 72 or 73.4 per cent of the 98 patients examined in the fifth or sixth month, 134 or 71.1 per cent of the patients tested in the seventh or eighth month and, finally, 49 or 74.2 per cent of those examined in the last month. Of the total of 400 patients studied, 288 or 72 per cent had a coagulation time ranging between one and five-tenths and two and five-tenths minutes.

Fig. 3 portrays concisely in graphic form the coagulation time in numerical frequency of the 400 gravid patients studied. It is observed that the coagulation times tend to group themselves in duration in the region of one and five-tenths to two and five-tenths minutes. It is to be especially noted that coagulation was completed in 349 or 87.2 per cent of these patients at or before two and five-tenths minutes, whereas only in 51 or 12.8 per cent of them was the time extended beyond two and five-tenths minutes.

In order to gain a clearer conception of the difference in the results obtained in the nonpregnant and pregnant individuals, comparative polygon graphs have been constructed based on the arrangement of the coagulation time values according to percentage frequency (Fig. 4). From these graphs one may note that there were considerable higher percentages of the rapid coagulation rate estimations (one and five-tenths to three minutes) among the gravid group of patients than among the nonpregnant. Although the clotting time readings for the entire number of individuals examined (pregnant as well as nongravid) may be considered to fall within the so-called normal range limits

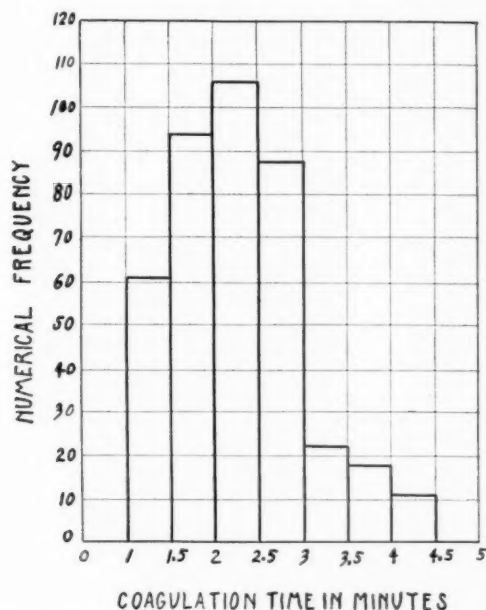


Fig. 3.—Histogram of grouped frequencies of coagulation time in 400 women in different periods of gestation.

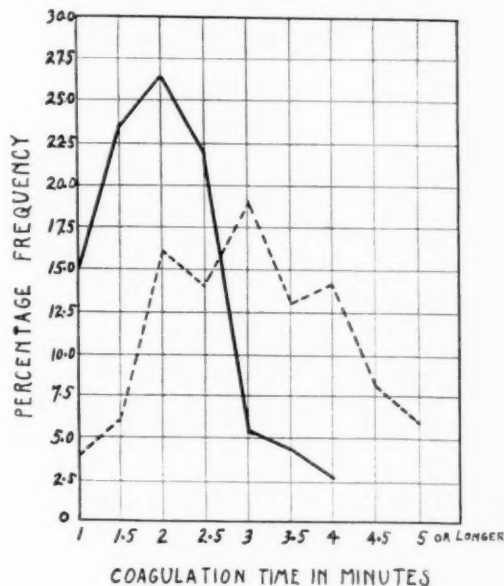


Fig. 4.—Comparative polygons of percentage frequency of coagulation time readings in (a) pregnant patients (solid line), and (b) normal nonpregnant individuals (broken line).

(there being no specific or fixed normal coagulation time), the results of the test suggest that there is an appreciable tendency of the blood to clot relatively more quickly in pregnancy than in the nongravid state.

The comparatively small differences in the clotting time in the two classes of women further suggests that the simple determination of the time required for a drop of blood to coagulate in vitro does not adequately represent the efficiency of the blood coagulating mechanism. It is, therefore, our belief that this ordinary test, in its present state of development, can not be relied upon to measure slight differences or changes in coagulability of the blood. Since the blood platelets and calcium salts, two of the necessary factors for proper coagulation, are not significantly altered in normal pregnancy, it seems that an estimation of the fibrinogen content, which is known to be definitely increased, would give more reliable information concerning the blood coagulability in this condition.

COAGULATION OF THE BLOOD POSTPARTUM

The coagulation tests of 100 individuals were performed within forty-eight hours, three to six days after childbirth, and again seven to ten days postpartum, in order to determine the immediate effect of parturition. Of the 100 patients studied in the puerperium, 76 per cent gave a clotting time of one and five-tenths to two and five-tenths minutes which corresponds in general with the findings of the aggregate number under study. In this limited group, the clotting time was one and five-tenths minutes in 26 patients, and two minutes in 35 patients. A large proportion of the conspicuously short coagulation times (one to two and five-tenths minutes) prior to delivery were distinctly lengthened in the lying-in period by at least fifteen seconds, while the primarily long clotting times remained the same, i. e., a change in time of less than fifteen seconds, or were, to a small degree, shortened. This slight, but positive, prolongation of the coagulating process would indicate a return of the values to those of the nonpregnant individual.

SUMMARY AND CONCLUSIONS

Tests for determinations of the coagulation time were performed on 100 nonpregnant women and on 400 gravid patients in the various periods of pregnancy. Additional tests were performed on 100 patients during the lying-in period.

It was found that only 36 per cent of 100 normal nongravid individuals gave a clotting time ranging between one and five-tenths and two and five-tenths minutes, whereas the coagulation was completed in 349 or 87.2 per cent of the 400 women examined in pregnancy before two and five-tenths minutes. On the basis of these results one may safely conclude that the coagulability of the blood (as shown by the test employed) is relatively increased in pregnancy.

Because of the small differences in the clotting time of the pregnant and nonpregnant individuals, it is the feeling of the authors that this test can not be relied upon to disclose the efficiency of the mechanism of coagulation.

The results of the test in the puerperal period show that there is a rather sharp tendency for the readings to return to the values found in the nongravid state.

The authors wish to acknowledge their appreciation to Miss Regina T. Hoban, who carefully performed all the determinations of coagulation time under the direct supervision of Doctor Baxter L. Crawford, Director of the Pathological Laboratory, Jefferson Medical College Hospital.

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THE LOWER SEGMENT CESAREAN SECTION, OR CELIOISTHMY

A PRELIMINARY REPORT

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THE performance of the newer types of cesarean section, namely the low or cervical, hinges on the knowledge of the extent, the structure, and the physiologic characteristics of the lower segment of the uterus. Though Bandl,¹ Küstner,² Bayer,³ Bumm and Blumreich,⁴ et al., hold that the lower segment is derived from the cervix, on the other hand Ruge,⁵ Schroeder,⁶ Veit,⁷ Zweifel⁸ and other investigators have proved either by frozen sections or tissue examinations that, at least in the latter months of pregnancy and at the onset of labor, it is derived only in part (2 to 3 cm.) from the cervix, while the larger portion (6 to 8 cm.) is developed from the lower zone of the body of the uterus; furthermore, Hofmeier⁹ has demonstrated by histologic researches a close similarity of structure between the lower segment and the uterine body; likewise on an anatomical basis, Aschoff,^{10, 11} has shown that the lower segment corresponds to that part of the uterine body which he calls "isthmus uteri" and Schmidt¹² and Stieve,^{13, 14} have pointed out that from the third month of gestation on, the isthmus changes its tubular shape and becomes unfolded to form the lower pole of the uterine cavity. During labor the uterus becomes differentiated into two distinct portions, divided from each other by means of the Bandl's or contraction ring. The upper, thicker, and harder corresponds to the active, contractile portion; the lower, thinner, and softer corresponds to the passive, distended isthmus, with which the cervix, in the gradual process of effacement brought about particularly by the upward and outward retraction of its muscular and elastic fibers, has become fused, so to speak. In this manner, the fully developed isthmus is formed and in such condition its length varies between 6 to 9 cm.

As De Lee states, "One may deliver a fetus by an incision through it (the lower segment) without encroaching on the contractile or motor portion of the uterus."¹⁵ This statement, while it may obtain for a fetus having a small head, in our experience does not hold true for the average

full-term child. As a matter of fact, in performing the laparotrachelotomy, as described by Beck and De Lee, in several instances we met with some difficulty in extracting the child, through the conventional 10 cm. incision, so that often tears resulted in the upper contractile portion of the uterine body, with consequent increased bleeding, and lessened chance of sound healing of the incision. On the other hand, Williams, in describing the technic of the classic cesarean section, points out that an incision in the uterine body measuring 15 cm. is necessary.¹⁶

The same author in describing the vaginal cesarean section states that: "When one recalls that the suboccipitobregmatic circumference of the fully developed head measures 32 cm., if only an anterior incision is made, it must measure 15 to 16 cm. in length to permit the passage of the head, without laceration of its upper end, which would necessitate opening the peritoneal cavity."¹⁷

There is no reason why the same criteria should not hold true and particularly so, in the performance of the low cesarean section, inasmuch as the latter operation involves a zone of the uterus, which during labor becomes quite thin and prone to laceration. In the face of such difference of opinion, however, and with the purpose of solving the problem of the length of the incision required for the delivery of the head of the full-term child, we have resorted to the following scheme, in which we have tried to reproduce as closely as possible the conditions as met with in the actual operation: A square piece of rubber dam, in which a slit 10 cm. long had been made, was passed over the suboccipitobregmatic circumference of each head of 50 newborn babies, shortly after delivery. From this experiment, which included newborn delivered normally, or by forceps, or by version or section, one could readily see that if the suboccipitobregmatic circumference was between 30 and 31 cm., the original line of incision in the rubber dam would invariably tear to not less than 11 cm., while if the same circumference was between 31 and 32 cm., the incision would be extended to 11 or 12 cm., and so on, proportionately, reaching as high as 14 or 15 cm. in some cases in which the suboccipitobregmatic circumference measured over 34 cm. The average suboccipitobregmatic circumference in the 50 cases was 32.2 cm.; the average incision required was 12.1 cm.

In performing a low cesarean, a child presenting by the head is not always delivered in the plane of the suboccipitobregmatic diameter and this is by no means a constant quantity. It may vary according to the sex or the race of the fetus, or to the degree of compressibility of the head or to the stage of ossification of the sutures, or to the extent of the molding, etc., yet for practical purposes one has to admit that the suboccipitobregmatic being the smallest circumference of the fetal head, the length of the incision through which this may be delivered, without causing injury or trauma to the uterine or pelvic structures, should at least be adequate to the above circumference.

By means of a preoperative pelvicephalometric roentgenogram, following the method of Thoms,¹⁸ one might get the exact measurements of the fetal cephalic diameters, but in practice, at the actual operation, after opening the abdominal cavity, one may obtain a fairly accurate idea of the size of the head by palpation, through the thin wall of the lower segment, and with sufficient experience may judge the extent of the incision.

As shown above, the length of the lower uterine segment is rarely above 10 cm., and the minimum requirement for the passage of the average full-term fetal head is 12 cm.; therefore, it is obvious that the longitudinal incision is inadequate for delivery. This observation led to the introduction of the transverse incision, a method first suggested by Kehrer in 1881, later described by Kerr and Hendry,¹⁹ and followed by Hirst,²⁰ Stein and Deventhal,²¹ Phaneuf,²² et al. In the average case, however, a rectilinear transverse incision of 10 cm. is inadequate for the delivery of the child, for in such circumstances, it is unavoidably followed by injury to important blood vessels (especially the uterine) or

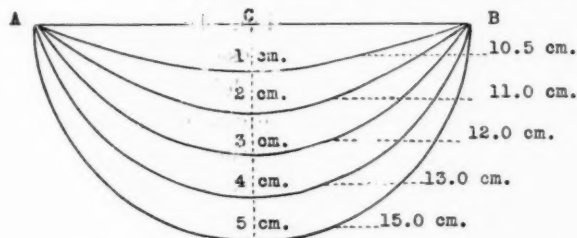


Fig. 1.—Diagram showing the proportionate increase in length of each arc in relation to its distance from the center of the cord.

even by laceration of the broad ligaments. Therefore, it has appeared to us that a transversely curved incision would be more satisfactory because it may be extended to 14 or 15 cm. without interfering with the contractile portion of the uterus or with important lateral structures. This is clearly shown by Fig. 1, in which, though the chord *AB* remains constant, 10 cm., yet, the different arcs starting from its terminal points *A* and *B* have a variable length, which is in direct proportion to the distance of their center from the midpoint *C* of the chord.

In as much as the field of the operation to be described is strictly confined within the limits of the isthmus, as defined above, it would seem proper to term the procedure "celioisthmotomy," or rather transverse celioisthmotomy in contradistinction to the longitudinal, provided the latter is also within the isthmus.

TECHNIC OF THE TRANSVERSE CELIOISTHOMOTOMY

The patient, prepared, catheterized and draped is anesthetized and placed in the Trendelenburg position. A longitudinal median abdominal incision about 15 cm. long is made from below the umbilicus to the symphysis pubis; the skin and subcutaneous tissues are retracted, the fascia divided some distance from the median line over the rectus muscle, which is either split longitudinally or retracted

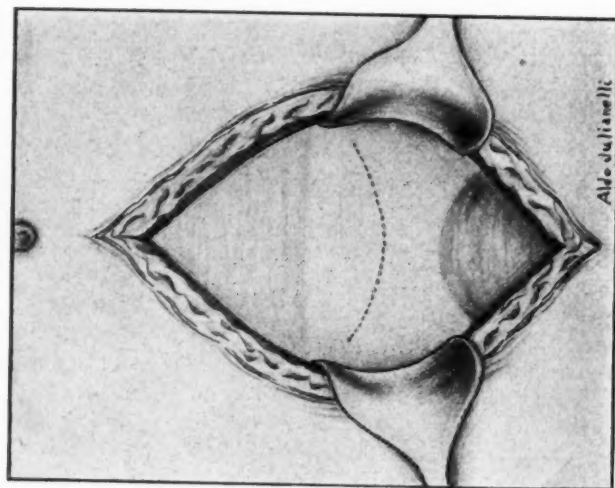


Fig. 2.—Intended line of incision in the loose peritoneum of the lower segment.

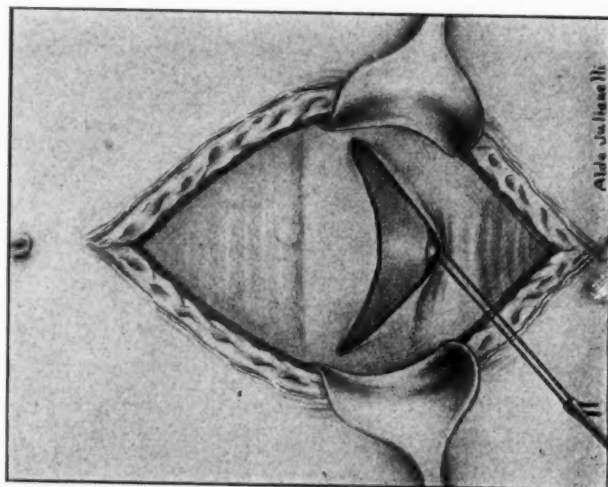


Fig. 3.—Transversely curved incision in the peritoneum of the lower segment.

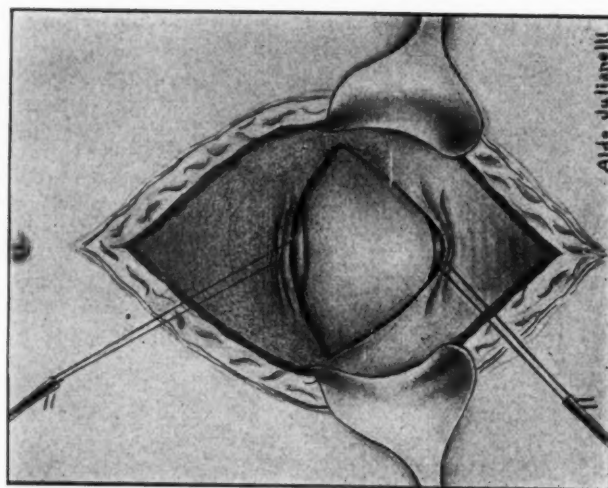


Fig. 4.—Two peritoneal flaps are raised and retracted by sutures.

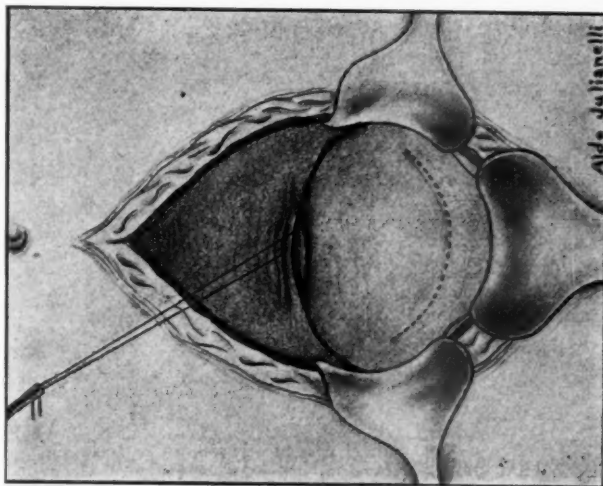


Fig. 5. — Intended line of incision in the lower segment.

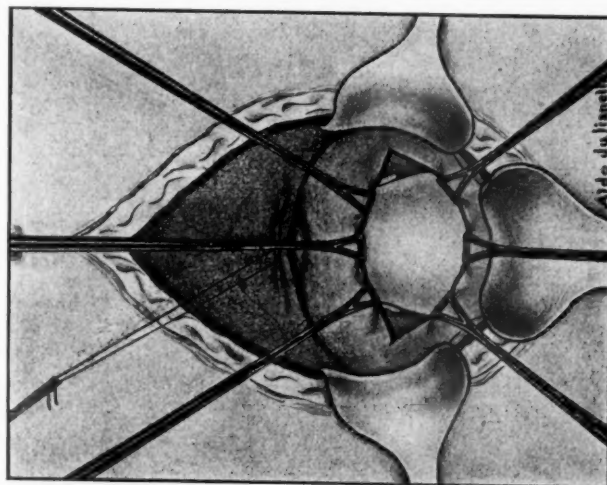


Fig. 6. — The incision in the lower segment completed and its edges caught with special clamps.

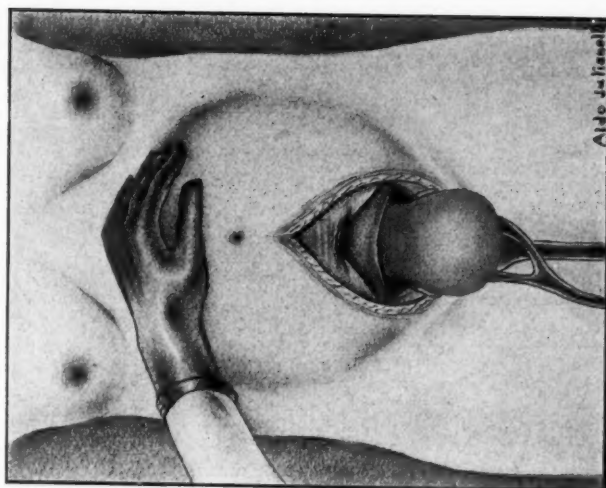


Fig. 7. — The child's head is delivered by pressure upon the fundus, over a single forceps blade used as a vectis.

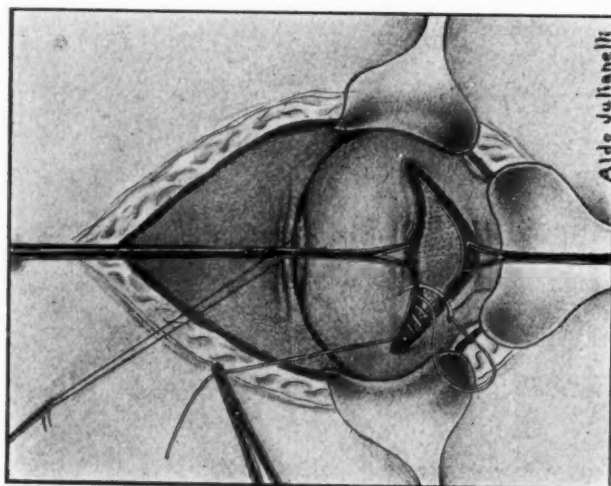


Fig. 8.—First row of sutures taking in the lower layer of myometrium.

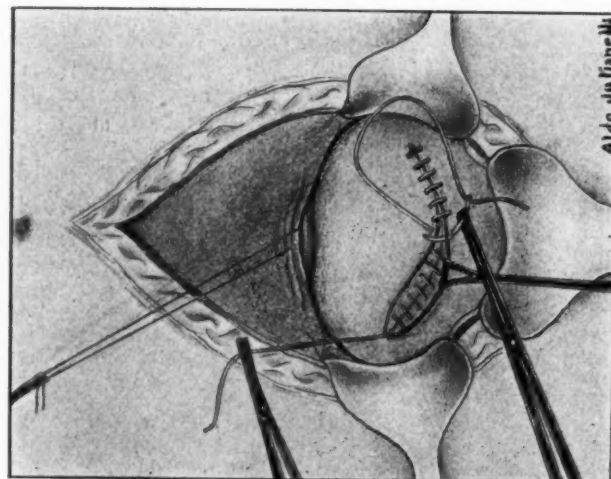


Fig. 9.—Second row of sutures taking in the upper layer of the myometrium and the fascia of the lower segment.

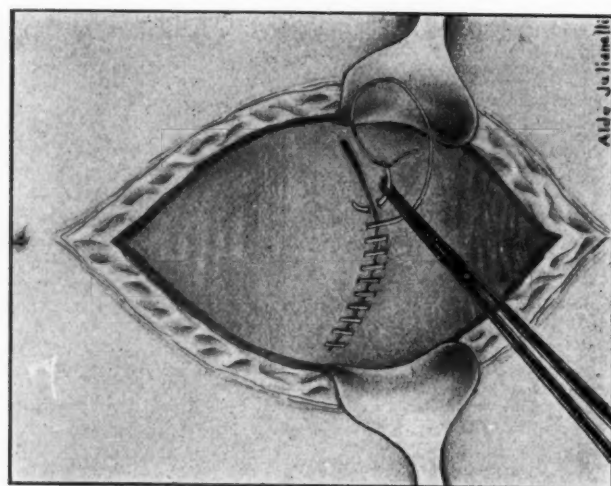


Fig. 10.—The edges of the peritoneum of the lower segment are directly united by a continuous suture.

outwards. The peritoneum is opened, special care being taken to avoid wounding the bladder, which is retracted over a protecting compress by a De Lee or Doyen retractor. The upper portion of the abdominal cavity is likewise packed off with laparotomy sponges, and two lateral retractors are slipped under the parietal peritoneum at both sides. A transversely curved incision, 12 to 15 cm. in length with the convexity downwards, is made through the loose uterine peritoneum, about midway between the "gray line," corresponding to the contraction ring, and vesical reflection, Figs. 2 and 3. By blunt dissection two peritoneal flaps are raised and their edges held out of the way by means of Allis forceps or preferably by traction sutures (Fig. 4). The bladder retractor is then placed over the lower flap, thus exposing the denuded lower uterine segment (Fig. 5). A transversely curved incision from 12 to 15 cm. long and with convexity downwards, is made in the lower uterine segment, starting at the center with a scalpel, and completing

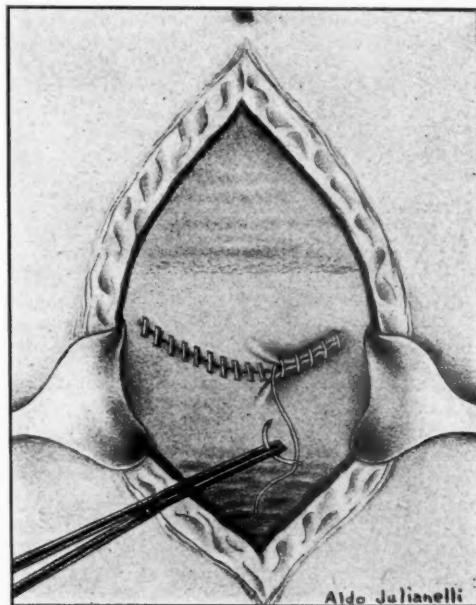


Fig. 11.—Additional row of continuous Lembert sutures, reinforcing the first line of sutures.

the incision on both sides with a pair of Mayo scissors. The edges of the incision are immediately caught with special triangular clamps, whose jaws grasp firmly but do not crush and devitalize the tissues (Fig. 6). As soon as the amniotic sac is opened, continuous aspiration of the fluid and blood is maintained by means of a suction apparatus. The baby's head is delivered by pressure on the fundus, over the palm of the hand, or a single forceps blade, used as an inclined plane (Fig. 7). In breech presentation the infant is extracted by the feet.

Immediately after the delivery of the child, 1 c.c. of pituitrin is administered to the mother by intramuscular injection. The placenta is allowed to separate spontaneously, unless there is some delay, when it is removed manually through the incision. In infected cases, however, if the cervix is known to be dilated sufficiently, the cord is dropped back into the uterus and placenta expressed by the Credé method through the vaginal canal, following the closure and peritonization of the incision.

The incision is closed with No. 2 chromic catgut continuous sutures, in two layers, the first including the lower layer of the muscular coat and at times the mucous membrane also, and the second taking in the upper layer of the myometrium and the fascia of the lower segment (Figs. 8 and 9).

In clean cases, the edges of the uterovesical peritoneum are united without flapping; in suspicious and unclean cases, however, we prefer to anchor the upper flap of the peritoneum to the lower segment with a few interrupted sutures and then raise the lower flap and suture it with a continuous No. 1 chromic catgut over the upper flap, in the manner described by Beck²³ and De Lee.²⁴ By thus covering the incision in the isthmus by means of the vesical peritoneal flap, the incision becomes sealed and leakage of infective material from the interior of the uterus to the peritoneal cavity is prevented. Moreover, in order to avoid adhesions to the lower segment we have preferred, lately, to unite the two peritoneal edges directly, reinforcing with an additional row of continuous Lembert sutures (Figs. 10 and 11). The abdomen is then closed in layers in the usual manner. In infected cases a rubber dam drain is placed under the skin, in the lower angle of the incision.

For the purpose of illustrating certain relevant features of both types of operation, a brief statistical review of twenty consecutive cases from our service, is given.

In chronologic order the cases were distributed as shown in Table I:

TABLE I. YEARLY INCIDENCE OF CELIOISTHOMOTOMIES

YEAR	1927	1928	1929	1930	1931
Longitudinal	3	4	3	3	1
Transverse	—	—	—	4	2

The indications are detailed in Table II.

TABLE II. INDICATIONS

	LONGITU- DINAL	TRANS- VERSE
Contracted pelvis, border line	6	—
Moderately contracted pelvis	4	2
Relatively contracted pelvis	—	1
Contracted pelvis, funnel type	1	—
Placenta previa centralis	1	—
High amputation of cervix	1	1
Congenital vaginal stenosis	—	1
Relatively contracted pelvis, repeated cesarean section	—	1
Vaginal atresia, septate vagina	1	—

All these cases had a long test of labor, except the case of longitudinal section done for high amputation of cervix and another, a cesarean section repeated for the fourth time, in the transverse series, both of which were performed in the beginning of labor.

Anesthetic.—Ether was used in ten cases (longitudinal), gas-oxygen and ether in seven cases (1 longitudinal, 6 transverse) and local infiltration with novocaine-adrenalin in three cases (longitudinal).

Mortality.—There was no mortality in either series. It is interesting

to note in this regard, that an excellent survey, recently made by Phaneuf,²⁵ shows a mortality of 5.6 per cent or nine maternal deaths in 160 cases, in which a longitudinal celioisthmotomy was performed, as against 3 per cent or six maternal deaths in 198 cases in which the transverse section was employed.

Morbidity.—The standard of morbidity varies with different institutions. We believe that a temperature ranging from 99.5° to 100° during the first two days postoperative, should be considered as a physiologic reaction following a celiotomy. Therefore, we have designated as *normal* those cases in which, during the first two days postoperative, the temperature does not exceed 100° by mouth; *mildly febrile* those cases in which the temperature ranges from 100° to 101°; *moderately febrile* when the temperature ranges from 101° to 103°; and *markedly febrile* when the temperature is above 103°.

Table III is based on the classification above:

TABLE III. RELATIVE MORBIDITY IN THE TWO TYPES OF CELIOISTHOMOTOMY

		LONGITUDINAL TYPE	TRANSVERSE TYPE
Normal		6 cases or 43%	3 or 50%
Febrile	Mildly	1 case or 7%	3 or 50%
	Moderately	7 cases or 50%	
	Markedly	0	0

By summing up the figures for the febrile cases in the two groups, it is found that there is a percentage of 57 per cent in the longitudinal cases, as against 50 per cent in the transverse cases.

Though the patients in the transverse group were in poorer condition than in the longitudinal, due to membranes ruptured for a longer period of time, or to larger number of vaginal examinations at home, or to instrumental attempts at delivery, yet, none showed a marked degree of morbidity, and as a matter of fact, there was less morbidity than in the longitudinal group.

TABLE IV. CAUSES OF MORBIDITY IN CELIOISTHOMOTOMY

	LONGITU- DINAL	TRANS- VERSE
1. Fat necrosis of lower angle of the wound	1	—
2. Long test of labor (aver. 39 hours)	3	—
3. Repeated vaginal examinations at home	3	1
4. Abscess of lower angle of incision and thrombophlebitis	—	1
5. Membranes ruptured for over 26 hrs. attempt at forceps extraction	—	1
6. Vaginal packing left in vagina for 12 hrs. in two cases of placenta previa centralis	1	—

We feel, however, that a comparative study of a larger series of celioisthmotomies is necessary before one may arrive at more definite conclusions about this often neglected phase.

COMMENTS

The celioisthmotomy is especially indicated in suspected or infected cases, in which labor has lasted many hours, the membranes ruptured, when questionable vaginal examinations and manual or instrumental manipulations have been done, when there is fever, and the amniotic fluid is malodorous. This has been shown by the studies of Beuttner,²⁶ Hauch,²⁷ Gaifami,²⁸ et al., and may be explained on the ground that the low uterine segment of a pregnant woman, as it has been demonstrated by Hofbauer,²⁹ is protected against infection by the presence, in the parametrium, of phagocytes (monocytes and clasmatocytes), whose number

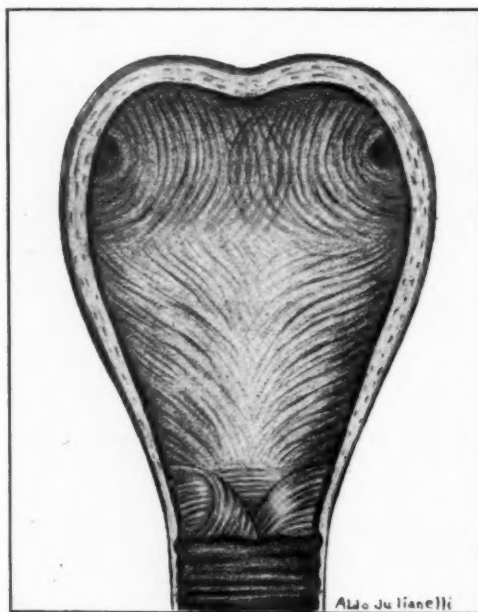


Fig. 12.—Dissection of uterine muscle, showing inner and outer layers of the isthmus. Adapted from Helle and Chenantais.

is increased by prolonged labor, and particularly by infection.* For this reason, in celioisthmotomy postoperative complications are much less frequent than after the classic section. As a matter of fact, peritonitis, gastric dilatation, and ileus are almost always absent. Adhesions are uncommon, and rupture of the scar, in a subsequent pregnancy or labor, a very rare occurrence. And an added advantage of isthmotomy is that it can be performed after a long test of labor, in cases of border line contracted pelvis.

In a recent survey of 874 cervical cesarean sections, Greenhill³⁰ stresses

*Nevertheless, we believe that in frankly infected cases, the Porro operation yields far better results than celioisthmotomy.

the fact that at the Chicago Lying-in Hospital, the laparotrachelotomy is the operation of choice when abdominal delivery is indicated. He refers particularly to the longitudinal type of low cesarean section inasmuch as there were only four cases in which the transverse method was employed. However, we feel that the latter method is preferable in the average case in which an incision of 12 cm. or more is necessary, whereas by employing the longitudinal method, a tear extending into the corporal portion of the uterus with consequent rupture of the circular sinus, at the junction of the upper and lower segments, would be unavoidable. The transverse crescentic incision in the lower uterine segment is also justified by the anatomical disposition of the muscle fibers (Fig. 12), as well as of the blood vessels (Fig. 13), whereby one may divide these tissues almost in



Fig. 13.—Pregnant Uterus with arteries and veins injected. (From C. Heitzmann, *Human Anatomy*.)

their line of cleavage, causing a minimum of trauma and hemorrhage. Furthermore, a close examination of Fig. 13 seems to disprove the opinion held by some operators that there is a median "avascular" zone of the uterus, which would permit an almost bloodless field in performing the longitudinal celioisthmotomy. Other advantages of the method are: the incision is *always* within the quiet zone of the uterus, and is often more accessible for suture; the spill is limited to the lowest portion of the abdominal cavity and is easily controllable, the head is delivered more readily; the omentum and intestines are, as a rule, out of sight and practically never handled; there is less tendency to postoperative abdominal hernia, and as far as the literature shows, less risk of rupture of the scar in a subsequent pregnancy or labor.

SUMMARY AND CONCLUSIONS

1. Experimental and surgical evidence shows that an incision measuring 12 cm. or more is necessary for the delivery of the average full-term child's head.

2. A longitudinal incision in the lower segment is, therefore, inadequate, and a transverse curvilinear incision must be employed if one is to limit the operative field to the quiet zone. As this is represented by the isthmus, the term "celioisthmotomy" is suggested as being more appropriate.

3. A description of the operative technic is given in detail, though no originality is claimed; the transverse celioisthmotomy, as outlined above, seems to possess decided anatomic, physiologic, and technical advantages over the longitudinal.

4. A brief review of 14 longitudinal and 6 transverse celioisthmotomies is given for the purpose of comparing certain relevant features. The mortality was nil in both groups, whereas, the morbidity was 57 per cent in the longitudinal group as against 50 per cent in the transverse, in spite of the larger number of poor risks in the latter.

5. A critical study of larger series of celioisthmotomies, laying stress particularly upon the "morbidity" phase, is necessary, before one may arrive at more definite conclusions about the relative merits of both types of operation.

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MALIGNANT OVARIAN NEOPLASMS*

WITH A REPORT OF THE END-RESULTS IN A SERIES OF 93 CASES

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THE present study is a brief review of all cases of malignant disease of the ovary which have been observed in the Department of Obstetrics and Gynecology of the Hospital of the University of Pennsylvania. From a former survey¹ of the Hospital records it was found that ovarian neoplasms constituted 7.7 per cent of all gynecologic lesions. Fourteen per cent of all newgrowths of the ovary were malignant. Clinical and pathologic records of 125 patients, operated upon in the Department form the basis for the study. These are supplemented by records of 28 tumors removed at other clinics, which were sent to the Departmental laboratory for diagnosis.

The results of the treatment of 93 patients, traced for three years or longer, are recorded.

MORTALITY

All patients were treated by operation. The operative mortality in the group of 125 patients, based upon all deaths from any cause, which occurred within thirty days of operation, was 13 (10.4 per cent). This group includes a number of exploratory sections. Not infrequently a patient is brought to the hospital suffering from an intraperitoneal tumor and an enormous amount of ascites. In the treatment of these patients, it has been our policy to make a small abdominal incision, often under local anesthesia, which permits evacuation of the ascitic fluid and results in the making of a positive diagnosis. If necessary, a small portion of the tumor is removed for a frozen section diagnosis. We have had a number of cases of this type which, prior to operation, were thought to be malignant, but which proved to be benign and were saved by removal of the tumor. In many, however, the preoperative diagnosis of advanced malignancy was confirmed, and although only a small incision was made and biopsy performed, they subsequently died, not as a result of operation, but from the progress of the disease, which was in a lethal stage at the time of operation. Many of these cases go to swell the operative mortality. These patients and others, who died of nonoperative conditions within thirty days of operation, constitute a considerable proportion of the operative deaths. If these deaths were excluded, the operative mortality would be greatly reduced. The actual operative mortality in ordinary cases is approximately 2 to 3 per cent.

*Read before the Philadelphia Obstetrical Society, October 1, 1931.

END-RESULTS

Of the 93 patients forming the basis for the end-result study, 50 or 53.8 per cent are known to be alive three or more years after operation. Of the 43 deaths, 29 patients died of recurrences of the malignant condition, and in the remaining 14, the cause of death was either from an intercurrent disease or unknown. The 43 deaths include all operative deaths in the entire series of 125 patients concerning whom any clinical information was available. As this analysis includes all operative deaths in the entire series of 125 cases, and the ultimate salvage is based upon the 93 traced cases, the proportion of three-year cures is somewhat greater than the figure 53.8 per cent would indicate. Most of the recurrences were pelvic in situation, the first symptom often being the development of ascites.

PATHOLOGIC STUDY

All tumors were submitted to histologic examination and for the purpose of study may be grouped as follows:

TABLE I. CLASSIFICATION OF TUMORS

	NUMBER	PER CENT
Specimens	153	100
Glandular carcinomas	90	58.8
Papillary carcinomas	54	35.2
Sarcomas	9	6.0

The glandular type was nearly twice as frequent as the papillary.

TABLE II. BILATERAL INVOLVEMENT ACCORDING TO TYPE OF TUMOR

TYPE OF TUMOR	NUMBER OF CASES	PER CENT BILATERAL
Glandular carcinomas	90	35.5
Papillary carcinomas	54	31.4
Sarcomas	9	22.2

All types exhibited bilateral involvement. There were 51 bilateral malignant tumors (34.2 per cent) of 149 records of malignant tumors. Of the 153 specimens studied, 4 were from patients who were operated upon a second time for recurrence.

FACTORS INFLUENCING END-RESULTS

There was a significant difference in the three year mortality rate according to the type of the tumor.

TABLE III. MORTALITY ACCORDING TO TYPE OF TUMOR*

TYPE OF TUMOR	NUMBER OF PATIENTS	PER CENT 3 YEAR MORTALITY
Glandular carcinomas	40	57.5
Papillary carcinomas	35	14.2
Sarcomas	5	40.0

*Excluding 13 deaths during first month after operation.

Table III shows the glandular carcinoma group, 42.5 per cent of the patients survived for three or more years, whereas, in the papillary group, the salvage over a like period was 85.8 per cent, or practically twice as great.

The relative three year mortality rate of patients having unilateral ovarian involvement, contrasted with those exhibiting bilateral ovarian malignant tumors, is of interest.

TABLE IV. RELATIVE MORTALITY. UNILATERAL VS. BILATERAL TUMORS

	NUMBER OF PATIENTS	PER CENT
		3 YEAR MORTALITY
Unilateral tumors	56	35.7
Bilateral tumors	24	41.6

The high incidence of bilateral involvement in the present series of cases, and its apparent relation to the proportion of three year salvages, raises questions of pathologic and clinical interest.

When only one ovary at the time of operation appears grossly malignant, may the other ovary also be microscopically malignant, but not grossly so? In 40 cases both ovaries were removed. In 33 of these cases both were microscopically and macroscopically malignant. The second ovary in 7 instances, however, though grossly benign in appearance, was microscopically malignant. It is apparent, therefore, that in these 7 cases (17.5 per cent) of the 40 under discussion, the macroscopic examination of the second ovary was insufficient for a complete diagnosis.

The influence of the extent of the operative procedure upon the proportion of three year salvage was also investigated. In 44 cases in which unilateral oophorectomy was performed, the three year salvage amounted to 34.1 per cent; whereas in 28 cases in which bilateral removal was carried out, the salvage for a similar length of time was increased to 53.5 per cent. The advantage of the more extensive operation, from this comparison is evident. This observation and the preceding one, dealing with the incidence of microscopic malignancy where the organ is grossly normal, demonstrate the advisability of performing bilateral oophorectomy in all cases.

A factor influencing the relatively high proportion of cases in which unilateral oophorectomy was performed was due in many instances to the fact that the malignant character of the tumor was recognized only upon histologic examination. This raises the important question of what should be the subsequent treatment of such a case. Distasteful as it may be to both patient and surgeon, our study would indicate a second operation is advisable in most cases. The mortality from a second operation will be not more than 2 or 3 per cent, whereas our figures indicate an increased salvage by such procedure of 53.5 as against 34.1 per cent, a definite gain, even after subtracting a probable 3 per cent mortality.

Viewed from another standpoint our study shows that 17.5 per cent of the 40 macroscopically benign ovaries, associated with malignant neoplasms of the opposite organ, were histologically malignant. Prophylaxis, however, is better than cure, and this study emphasizes the necessity of carefully examining at the operating table both ovaries of patients in which unilateral oophorectomy is considered, and in many cases employing the frozen section method before closing the abdomen.

One feature of the study was the finding of a large number of uteri (14) exhibiting malignant invasion of the corpus. (Table V.) There was a significant relation between this complication and the three year mortality. Of 82 patients without uterine involvement, the three year mortality was 43.8 per cent; whereas, in 11 cases with involvement, the rate was 63.6 per cent, a percentage difference of 19.8. The number of patients with uterine involvement on the other hand was, for statistical purposes, rather small.

TABLE V. THREE YEAR MORTALITY OF PATIENTS WITH ASSOCIATED UTERINE CARCINOMA

	NUMBER OF PATIENTS	PER CENT 3 YEAR MORTALITY
Without uterine carcinoma	82	43.8
Associated uterine carcinoma	11	63.6

The relation of the gross appearance of the malignant ovary to the three year mortality was investigated. Table VI suggests the influence which the presence of adhesions may bear to ultimate salvage.

TABLE VI. RELATION OF OVARIAN ADHESIONS TO END-RESULTS

	NUMBER OF PATIENTS	PER CENT 3 YEAR SALVAGE
No adhesions	15	80.0
Adhesions present	32	56.2

From a glance it will be seen that there is a percentage difference of 23.8 between the two groups. This difference is large enough to be significant.

SUMMARY AND CONCLUSIONS

1. Observations upon 153 malignant ovarian neoplasms, in 125 operated patients, and upon 93 of the latter which were kept under observation for three years or more are recorded.
2. Of 125 patients, 13 (10.4 per cent) died within thirty days of operation.
3. Of 93 patients traced for three years or more, 50 or 53.8 per cent, were apparently cured.
4. In the entire series of 153 specimens, the glandular type of ovarian carcinoma was nearly twice as frequent as the papillary type.

5. In our group of 80 follow-up patients, not including 13 who died within one month of operation, the glandular type was four times as malignant as the papillary type and the latter less malignant than the sarcomas.

6. Thirty-four and two-tenths per cent of 149 malignant tumors were bilateral. The difference between 149 and 153 specimens (Conclusion, 1) is accounted for by 2 operations on each of four patients.

7. All types of tumor had approximately the same tendency toward bilateral involvement.

8. In 80 cases, bilateral involvement, regardless of type, showed a higher three year mortality than the unilateral type.

9. When one ovary was *grossly* malignant at the time of operation (40 cases), the other ovary was found to be grossly benign, but *histologically* malignant in 17.5 per cent.

10. The percentage of three year salvage is higher following bilateral than after unilateral oophorectomy, in the proportion of 53.5 per cent to 34.1 per cent.

11. Uterine involvement of the corpus is a relatively frequent accompaniment of ovarian carcinoma; patients exhibiting this complication present an increased three year mortality. This further emphasizes the importance of a radical operation.

12. Patients with malignant ovaries, the seat of surface adhesions, removed at operation, exhibit a higher three year mortality than do those which present a smooth surface at this time.

13. Even advanced cases should receive the benefit of an exploratory section. This may be performed under local anesthesia. It permits relief of ascites, and histologic confirmation of diagnosis. By this policy occasionally supposed malignant conditions are found to be benign and such patients may be saved by an appropriate operation.

14. Bilateral oophorectomy and removal of the uterus should be the operation of choice, even though the second ovary appears to be grossly benign.

15. At the operating table all macroscopically benign ovarian tumors should be carefully examined. If necessary, when a unilateral oophorectomy is contemplated, a frozen section should be made, and everything possible should be done to exclude malignancy, before the abdomen is closed, and if malignancy is found, hysterectomy and a bilateral oophorectomy is the operation of choice.

REFERENCE

- (1) Norris, C. C., and Vogt, M. E.: AM. J. OBST. & GYNEC. 10: 684-692, 1925.
133 SOUTH THIRTY-SIXTH STREET. (For discussion, see page 911.)

END-RESULTS OF RADIUM THERAPY IN CARCINOMA OF THE CERVIX*

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THIS report summarizes the end-results obtained by radium therapy in 475 cases of carcinoma of the cervix admitted to the Gynecological Service of the Hospital of the University of Pennsylvania from 1913 to July 1, 1926. Follow-up data were obtained in 89.15 per cent.

TABLE I. CASES OF CARCINOMA OF THE CERVIX, JANUARY, 1913, TO JULY, 1926

	NUMBER	PER CENT
Total number of patients	479	
Patients treated with radium	475	99.16
Patients seen but not treated*	4	0.83
Patients traced	427	89.15

*Three cases too extensive for treatment.
One patient refused radium treatment.

During the first few years covered by this report, all operable cases were treated by panhysterectomy, and radium was used only in the more advanced stages. This fact accounts in part, at least, for a somewhat lower percentage of favorable five-year end-results than have been recently reported by clinics in which radium has been used to the exclusion of operation. During the past eleven years, only one patient with carcinoma of the cervix has been operated upon; the remainder have been treated exclusively by radiation.

In grouping the cases we have followed the classification proposed by Schmitz. As shown in Table II, over four-fifths of the cases were in the so-called inoperable group and in only one-fifth was the disease either definitely or questionably limited to the cervix.

TABLE II. CLASSIFICATION BASED ON EXTENT OF DISEASE

	NUMBER	PER CENT
Total patients seen	479	
Early Lesions	92	19.20
Stage I	58	12.10
Stage II	34	7.09
Advanced Lesions	387	80.80
Stage III	244	50.93
Stage IV	63	13.15
Stage V	52	10.85
Extent not stated	28	5.84

Three patients died shortly after treatment, giving a primary mortality of 0.63 per cent.

*Read at a meeting of the Obstetrical Society of Philadelphia, October 1, 1931.

TABLE III. PRIMARY MORTALITY IN RADIUM CASES

	NUMBER	PER CENT
Total patients treated with radium (Either radium alone or cautery and radium)	475	
Primary Mortality	3	0.63
<i>Deaths:</i>		
Case 12936. Stage I. Cautery amputation and radium, 2400 mg. hr. Died of pulmonary embolism on sixth day.		
Case 8599. Stage III. Radium, 2400 mg. hr. Died of septicemia on fourteenth day.		
Case 11293. Stage III. Radium, 1640 mg. hr. Died of pelvic peritonitis on twenty-seventh day.		

The five-year end-results for the entire series are shown in Table IV. The classification of untraced cases is controversial, but in this report we have included them among those who died of carcinoma. Eleven patients who lived five years or more but who eventually died of the disease are, of course, not included in our percentage of five-year cures. Sixty-

TABLE IV. FIVE-YEAR END-RESULTS IN PATIENTS TREATED WITH RADIUM

Total patients applying for treatment	479
Total patients treated	475
Total patients living 5 or more years	73
Absolute 5-year cure rate	15.24%
Relative 5-year cure rate	15.36%

seven patients are living and apparently cured at the time of this report (October 1, 1931). Six additional patients who lived five or more years but who died of some condition other than carcinoma are counted as five-year cures. Following is a brief résumé of these cases:

1. Case 4899. Lived seven years after treatment. Her physician reported that there was no trace of carcinoma at the time of her death. Died at age of sixty-three.
2. Case 14372. Stage II. Lived five years after treatment. Died of heart disease at age of sixty-seven.
3. Case 6353. Stage III. Lived five years after treatment. Died of intestinal obstruction at age of seventy-five. Her physician reported that there was "no trace of carcinoma after treatment."
4. Case 9518. Stage III. Lived ten years after treatment. On last examination, Dr. Clark found her "a complete seven-year cure." Died at age of sixty-two.
5. Case 6592. Stage III. Lived thirteen years after treatment. Died of heart disease at age of sixty-seven.
6. Case 8628. Stage V. Lived six years after treatment. Died of "stroke" at age of sixty.

The results obtained in the various stages of the disease are given in Tables V and VI. This shows that in Stages I and II, which form the so-called operable group, cure has resulted in approximately one out of three; in 387 definitely inoperable cases the salvage has been about one out of ten.

Contrary to the opinion of others we believe that high amputation of the cervix with the cautery or radio-knife and the immediate application of radium are advantageous in the treatment of early carcinoma of the cervix. This may be attended by increased morbidity as well as mor-

TABLE V. FIVE-YEAR END-RESULTS ACCORDING TO DEGREE OF EXTENSION

STAGE	TOTAL NO. PATIENTS	PATIENTS TREATED	PATIENTS LIVING 5 OR MORE YEARS	ABSOLUTE CURE RATE	RELATIVE CURE RATE
I	58	58	23	39.65%	39.65%
II	34	34	7	20.58%	20.58%
III	244	243	32	13.11%	13.16%
IV	63	60	3	4.76%	5.00%
V	52	52	6	11.53%	11.53%
Not stated	28	28	2	7.14%	7.14%

TABLE VI. FIVE-YEAR END-RESULTS ACCORDING TO OPERABILITY IN PATIENTS TREATED WITH RADIUM

	NO. PATIENTS	NUMBER LIVING	ABSOLUTE 5-YEAR CURE RATE
Operable cases	479	73	15.24%
(Stages I and II)	92	30	32.60%
Inoperable cases	387	43	11.14%

tality, and, theoretically, it may be justly criticized on the ground that dissemination of the disease is favored, but the fact that approximately 53 per cent of our Stage I cases treated by this method were cured argues strongly in its favor.

TABLE VII. FIVE-YEAR END-RESULTS IN STAGE I CASES TREATED BY AMPUTATION AND RADIUM

Number Stage I cases so treated	34
Number patients living 5 or more years	18 or 52.94%

In his papers on the subject, Dr. Clark repeatedly expressed the belief that the chief benefit is derived from the initial radium treatment but he advocated reradiation on the appearance of active disease, and this plan has been followed by those of us who were associated with him.

During the earlier years covered by this report the routine treatment consisted of 2400 mg. hr. of radium followed by a similar dosage in six weeks. During the past few years the second routine application has been omitted. One hundred milligrams of radium has been used, filtered by 1 mm. of silver or 2 mm. of brass and soft rubber tubing. Re-radiation has been employed only in those patients showing evidence of continued growth. While in properly selected cases reradiation is undoubtedly of value as a palliative measure, Table VIII shows that it has not increased the percentage of cures.

Table IX shows the number of patients living beyond the five-year period and the absolute cure rate for each yearly series from five to eighteen years after treatment.

TABLE VIII. END-RESULTS ACCORDING TO NUMBER OF RADIUM TREATMENTS

NUMBER OF TREATMENTS	PATIENTS TREATED	NO. LIVING 5 OR MORE YEARS	PER CENT LIVING 5 OR MORE YEARS
One treatment	270	45	16.66%
Two treatments	167	25	14.97%
Three treatments	34	3	8.82%
Four treatments	2	0	
Five treatments	2	0	
Total	475	73	15.36%

TABLE IX. END-RESULTS OF CASES BEYOND FIVE YEARS, RADIUM GROUP
(479 CASES)

INTERVAL SINCE TREATMENT	CASES SEEN	PATIENTS LIVING 5 OR MORE YEARS	ABSOLUTE PER CENT 5-YEAR CURES
5 year	479	73	15.24%
6 year	457	64	14. %
7 year	411	56	13.62%
8 year	381	47	12.33%
9 year	337	40	11.86%
10 year	304	34	11.18%
11 year	263	31	11.78%
12 year	211	24	11.37%
13 year	156	19	12.17%
14 year	119	15	13.02%
15 year	78	12	15.38%
16 year	28	3	10.71%
17 year	11	3	27.27%
18 year	2	2	100. %

The biopsy material from 168 patients who were treated five or more years ago has been graded according to the classification of Martzloff. The selection of cases for this study has been impartial, as the only criterion was well preserved tissue for histologic study. Table X shows the results obtained in each of the histologic types.

TABLE X. END-RESULTS ACCORDING TO HISTOLOGIC TYPE

HISTOLOGIC TYPE (MARTZLOFF)	TOTAL NUMBER	NUMBER LIVING 5 OR MORE YEARS	PER CENT 5-YEAR CURES
Spindle cell	23	3	13.05
Transitional cell	30	8	26.66
Prickle cell	87	16	18.39
Adenocarcinoma	28	5	17.85

The striking feature of this analysis is the low curability rate in the spindle cell type which is recognized as being highly radiosensitive. This would seem to indicate that, so far as cure is concerned, its high degree of malignancy is of greater prognostic import than its radiosensitivity. The best results were obtained in the transitional cell group, which may be explained by its decreased malignancy as compared to the spindle cell type and its lessened radioresistance as compared to the prickle and adenoma types. Also of interest is the fact that the results obtained in adenocarcinomas were practically the same as those in the epidermoid group.

The evaluation of any treatment for carcinoma of the cervix must be based on the total salvage; by this we mean the number of cases cured as compared to the total number presenting themselves for treatment. The above report summarizes the results obtained in the John G. Clark Clinic since radium treatment was instituted eighteen years ago and includes all cases so treated from 1913 to 1926. The total salvage for the entire series has been 15.24 per cent.

During the first half of this period, however, radium was used only in the more advanced lesions and the curability for this period was 11.37 per cent. From 1920 to 1926 both early and late cases received radium treatment, with a salvage of 18.28 per cent. This compares favorably with the results reported from other clinics and confirms Healy's statement that, irrespective of the type of treatment used, the total salvage in any large series of cases will be in the neighborhood of 20 per cent.

Comparison of our results in Stages I and II with those from other clinics shows that our percentage of five-year cures is low and this may be due, in large part, to the fact that this clinic has advocated rather small radium dosage.

In this series of cases only five have received deep x-ray therapy in addition to radium. More recently we have subjected a number of patients to x-ray therapy and thus far our experience has been disappointing. However, the reports from other clinics unquestionably show its value as a palliative measure and encourage the hope that by its use in conjunction with radium the percentage of cures will be increased.

133 SOUTH THIRTY-SIXTH STREET.
1907 SPRUCE STREET.

(For discussion, see page 912)

Deilmann: Blood Typing in Mothers and Their Newborn. *Ztschr. f. Geburtsh. u. Gynäk.* 96: 102, 1929.

Deilmann typed the maternal and cord blood of 150 women and their newborn children. He found no defective types in the mothers and no variations from the Bernstein rule among the children.

LESTER E. FRANKENTHAL, JR.

Nishizaki, S.: Skin Pigmentation During Pregnancy. Its Significance for Parturition. *Japanese J. Obst. & Gynec.* 12: 390, 1929.

Nishizaki studied the skin pigmentation of 497 women in labor and found that those with intense skin pigmentation whether primiparas or multiparas often have shorter labors than other women. Likewise those with marked pigmentation less frequently have weak pains or require aid during delivery. They have less hemorrhage than women with little pigmentation and also fewer perineal lacerations. These facts indicate that women with intensive pigmentation are better prepared for labor than women with only slight pigmentation.

J. P. GREENHILL.

THE SPECIFIC GRAVITY OF THE BLOOD IN PREGNANCY AND IN THE PUERPERIUM*

A STUDY OF SEVENTY-FIVE PATIENTS

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THE following is a study of the anemia of pregnancy and of the puerperium in terms of the specific gravity of the blood. The falling drop technic of Barbour and Hamilton¹ was used as follows: "A drop of blood of definite size is released below the surface of a nonmiscible mixture. Its rate of fall depends on its density, which can be easily calculated as soon as the rate of fall of a similar drop of standard solution of known density (released under identical conditions) is available for comparison." I have employed this technic in various studies^{2,3} during the past five years, and I am convinced that it is a delicately accurate method of practical clinical value.

Search of the literature as far back as 1890 fails to reveal any work done on the specific gravity of the blood in pregnancy nor in the puerperium.

The average normal specific gravity of the blood in females in the afternoon is 1.053 (Schmaltz,⁴ Lyonnet,⁵ Leake, Kohl, and Stebbins,⁶ Polowe²). The present study is based on observations made between two and four o'clock in the afternoon. To make the tables more comprehensible, only the last two figures of the specific gravity values are used; thus a reading of 1.053 is represented by the figure 53.

Table I exhibits the findings in 75 patients. Fifty-two patients were observed during pregnancy, 40 patients in the puerperium (first ten days only), while 17 patients were followed through pregnancy and the puerperium. A total of 172 observations were made over a period of fifteen months, at one to four week intervals.

(a) *Pregnancy (52 Patients, 99 Observations).*—Experience has taught me that a specific gravity of the blood below 1.050 represents an anemic condition. If this figure is accepted as the lower limit of normal blood density, we find that 66 per cent of the observations made in the first trimester exhibit the anemia of pregnancy, 70 per cent in the second trimester, and 83 per cent in the third trimester.

Sixty-nine per cent exhibit the anemia of pregnancy in the first six months, while 79 per cent of the observations for the whole nine months of gestation represents definite grades of anemia.

The seventh month of gestation stands out as the month in which 100 per cent of the observations registers some grade of anemia.

(b) *The Puerperium (40 Patients, 73 Observations).*—There is no striking change in the specific gravity of the blood in the puerperium over that of pregnancy. If anything, the anemia is more marked and is present in a greater percentage (85 per cent) of the observations than during pregnancy.

*This work has been aided by a grant from the Committee on Scientific Research of the American Medical Association.

TABLE I. THE SPECIFIC GRAVITY OF THE BLOOD IN PREGNANCY AND IN THE PUERPERIUM

MONTH OF GESTATION								DAYS POSTPARTUM									
2	3	4	5	6	7	8	9	1	2	3	4	5	6	7	8	9	10
48	43	45	41	39	33	33	32	38	34	31	38	36	40	49	31	40	32
	44	47	47	40	41	38	37	43	40	37	43	46	40	50	39	43	36
	47	48	48	42	41	38	41	44	43	43	44		43	52	40	43	44
	51	50	48	44	42	42	41	46	43	45	45		43		43	44	47
	52	50	51	45	42	43	42	49	43	47	49		44		44	45	53
		53	52	46	43	43	42	50	44	47	52		45		44	45	
				48	44	44	43		46	48			46		50	46	
				49	45	46	43		46	49			47			46	
				49	45	46	44		48	49			48			48	
				51	45	47	44		49				48			49	
				52	47	47	44		50				52			52	
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Table II (17 patients, 31 observations in pregnancy, 22 observations in the puerperium) is presented so that it may be seen that the findings therein approximate closely the independent observations shown in Table I. No comment seems necessary.

In Table III (12 patients, 16 per cent of the total number observed who had a specific gravity of the blood below 1.040 at one time or another during pregnancy or during the puerperium) only 3 patients (25 per cent) had uneventful courses. In 3 cases (25 per cent) notations appear upon the histories that spontaneous lacerations had occurred, episiotomy, the application of forceps, or combinations of these. Six patients (50 per cent) of this series of low blood densities, proved to be decidedly pathologic on the part of the mother, the fetus, or both.

COMMENT

Any discussion of the specific gravity of the blood presupposes the idea that a change in the blood is at once manifested by a change in its specific gravity. Such a change may be brought about by an alteration in the number of erythrocytes, leucocytes, platelets; by alteration of the

TABLE II. THE SPECIFIC GRAVITY OF THE BLOOD IN 17 PATIENTS WHO WERE FOLLOWED THROUGH PREGNANCY AND THROUGH THE PUERPERIUM

PT.	OBSERVATION	MO. GEST.	DAYS POSTPARTUM	SP. GR. BLOOD
1	11	7		1.047
	26	7½		43
	22		3	47
	26		10	47
2	64	8		45
	61		4	52
3	63	9		44
	57		3	45
4	22	8		47
	37	9		52
	18		7	52
5	15	7		47
	34	8		43
	15		4	43
6	48	7		48
	55	8		47
	36		9	40
7	56	7		49
	61	9		44
	40		2	49
8	67	9		47
	55		6	47
9	34	9		47
	90	9½		43
	69		6	43
10	18	4		50
	39	5		47
	54	7		45
	41		6	48
11	14	8		50
	28	9		49
	13		3	48
	17		10	49
	24		23	46
12	74	8		51
	81	8½		43
	65		10	53
13	57	7		33
	59	8		37
	65	9		32
	43		3	37
	47		10	32
14	17	3		52
	30	4		50
	60		2	34
	62		9	43
15	42	8		45
	46	9		43
	32		6	43
16	43	9		44
	34		6	48
17	2	9		37
	21		9	42

TABLE III. A BRIEF OUTLINE OF 12 PATIENTS WHO EXHIBITED A SPECIFIC GRAVITY OF THE BLOOD BELOW 1.040 AT SOME TIME DURING PREGNANCY OR DURING THE PUERPERIUM

PATIENT	OBSERVATION	SPECIFIC GRAVITY OF BLOOD	MONTHS GESTATION	DAYS POST-PARTUM	REMARKS (NOTES FOUND ON HISTORIES OF RESPECTIVE PATIENTS)
1	88	1.039	6		Course uneventful. Discharged tenth day postpartum.
2	76	38	8		Course uneventful.
3	50	36		5	Weight of baby 5 pounds 6½ ounces. Course uneventful.
4	39	31		8	Low forceps; episiotomy; second degree laceration.
5	48	31		3	Low forceps; no damage to mother or child.
6	60	34		2	Second degree laceration. Un- eventful puerperium.
	62	43		9	Patient discharged tenth day postpartum in good condition.
7	58	39		8	Baby stillborn. Diagnosis: Toxemia from dead fetus. Wassermann negative. Fetal heart not heard three days prior to delivery. Temperature 104° nine hours before delivery.
8	59	38		4	Pyelitis of pregnancy. Temperature 101° to 104°. Condition cleared up after delivery, and the patient was discharged in good condition on tenth day postpartum. Weight of baby 5 pounds 7 ounces.
9	57	33	7		Grav. i. Blood pressure, 140/100. Albumin two-plus; Blood pressure 140/100. Weight decreasing.
	59	37	8		Albumin three-plus. Hemoglobin 43 per cent.
	65	33	9		Baby died on third day.
	43	37		3	Summary: Patient admitted about one month before expected date of delivery, because of dizziness, headache, weakness, edema of ankles, etc. She delivered spontaneously a premature infant weighing 4 pounds 4 ounces; infant died on third day. After discharge patient was referred to the medical clinic for observation. Electrocardiograph: tachycardia.
	47	32		10	
10	2	37	9		Toxemia of pregnancy. Blood pressure 210 systolic.
	21	42		9	Weight of baby 9 pounds 5½ ounces. Wassermann negative. On dietary régime blood pressure lowered markedly. Puerperium uneventful. No rise in blood pressure, though blood count revealed secondary anemia. Electrocardiograph revealed no evidence of myocardial pathology.

TABLE III (CONTINUED)

PATIENT	OBSERVATION	SPECIFIC GRAVITY OF BLOOD	MONTHS GESTATION	DAYS POST-PARTUM	REMARKS (NOTES FOUND ON HISTORIES OF RESPECTIVE PATIENTS)
11	14	36		10	Grav. ii. Twin delivery. One stillborn. Red blood count 3.2 mil. Hemoglobin 40 per cent. <i>Summary:</i> Adherent placenta. Second degree laceration. First delivery vertex. Second breech, forty-five minutes later. Placenta was adherent and took three hours for removal. Credé and saline injections into cord first tried and were unsuccessful. Manual removal finally resorted to. Aside from a definite anemia the first week, patient discharged in fairly good condition. Wassermann negative.
12	26	39		80	Grav. ii. Perineal and cervical lacerations. Infant died on ninth day; found to have dextrocardia.

hemoglobin content, fibrinogen content, ash content; by shifting water balances; by alteration of lipoid values.

In pregnancy and in the puerperium no one factor alone may be incriminated as the sole agent which so materially affects the weight of the blood. The demands of fetal development are reflected in the altered content of the mother's blood, all of the separate constituents of which are affected, normally, in proper proportions and such alterations are reflected in the specific gravity of the whole blood. Any deviation downward of the physiologic anemia of pregnancy and of the puerperium should herald some pathologic change. However, due regard should be given one's clinical judgment in evaluating the specific gravity of the blood in any given case.

SUMMARY

- a. Low specific gravity values may be of aid in differentiating between pregnancy and uncomplicated tumor of the uterus.
- b. When the mother's blood density falls below 1.040, the complications of pregnancy and of the puerperium should be looked for.
- c. One reason for the increased anemia of the puerperium may be the attendant hemorrhage at delivery. Another reason may be that active lactation may alter the water and mineral balance so as to prolong and intensify the anemia throughout the nursing period, such anemia diminishing as lactation diminishes.
- d. A teleologic theory as to the origin of amniotic fluid: Sakuma⁷ injected 10 to 20 c.c. of 1 per cent to 2 per cent solutions of pigments into the ears of gravid rabbits. He found that only the acid types of pigments (trypan red, trypan blue, Congo red, rose bengal, and one or two

others) passed through the amniotic epithelium. The pigment was found in the amniotic epithelium, in the amniotic fluid, in the fetal intestines, but not in the kidney substance of the fetus. He concludes that the passage of the pigment is brought about directly from the maternal body and not by excretion on the part of the fetus.

The anemia of pregnancy is apparently at its height during the seventh month of gestation. In this connection it is of interest to note that Kamei⁸ determined the specific gravity of amniotic fluid in the chick and found it greatest toward the end of embryonic development. This may have some bearing on the nutrition of the embryo, possibly the mineral supply, an increase of which in the amniotic fluid would raise its density, a withdrawal of which from the mother's blood stream would lower her blood density.

In a previous publication³ I commented upon the specific gravity of the blood in 14 cases of fluid collections. All the cases, eight in number, in that series which exhibited blood densities below 1.050 presented free fluid in serous cavities. I was quite impressed by these findings and felt at the time that some extraordinary changes must take place in blood density before free fluid finds its way into serous cavities.

If it is true that the specific gravity of the blood must be altered downward in order to effect a transudation of free fluid into serous cavities, then it would seem that the anemia of pregnancy must be a true physiologic phenomenon, one of the objects of which is to bring about the transudation of amniotic fluid through the amniotic epithelium.

e. The results by the falling drop technic lend themselves to comparison with the sedimentation test in pregnancy and in the puerperium. Bland, Goldstein, and First⁹ have studied a large series of cases. Suffice it to say that the results by both methods are in fair agreement, the practical advantage, I feel, lying with the falling drop method because the determination may be made in two minutes' time.

CONCLUSIONS

a. The falling drop technic for determining the specific gravity of fluids offers an easy, rapid, and accurate orientation as to the status of the blood at any moment.

b. The physiologic anemia of pregnancy was found generally to be represented by specific gravity values of the whole blood between 1.050 and 1.040.

c. The pathologic anemias of pregnancy and of the puerperium are more apt to be represented by specific gravity values of the whole blood below 1.040. However, one's clinical judgment should always prevail.

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555 EAST TWENTY-SEVENTH STREET

INTRAPERITONEAL HEMORRHAGE OF OVARIAN ORIGIN*

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THIS report is based upon 26 cases in which intraperitoneal hemorrhage was noted by the operating surgeons. Fourteen are taken from the records of the Woman's Hospital, while the remaining 12 patients were operated upon in other hospitals in and outside New York City.

* * * *

FREQUENCY

Efforts to determine the incidence of hemorrhage of ovarian origin have been disappointing. In the first place the hospital index-headings do not bring these cases into the open and they are variously sequestered under "cyst of ovary" or as chronic appendicitis, chronic salpingitis, or oophoritis; oophorectomy, resection of ovary, appendectomy, etc. Secondly there are many hemorrhages of minimal degree, insufficient to produce symptoms. Among 992 cases with diagnosis "cyst of ovary" at Woman's Hospital during the five years 1926 to 1930 inclusive, there were eleven cases or 1.1 per cent where blood in the peritoneal cavity was noted at operation, an additional seven cases where the bleeding followed the operative manipulation itself, and three more in which rupture was believed to have occurred at the vaginal preparation for operation, a total of 21 cases (2.1 per cent). The series contained 288 cases of microcystic disease of ovary with bleeding in four (1.4 per cent); 11 cases of dermoid and 11 cases of papillary cyst with bleeding in none. Torsion of the pedicle occurred eleven times, with bleeding in 2 cases at the Woman's Hospital. Warthin found 6 cases from 1895 to 1920 on the Pathological Service of the University of Michigan. Simon found the incidence of ovarian bleeding to vary from 0.33 per cent to 1.04 per cent of all laparotomies on the surgical and gynecologic divisions of Mörby Hospital. Caverly in a recent review of 83 ovarian cysts found hemorrhage into the cyst in 18 per cent but no case of rupture or free bleeding; but in the five-year period studied at Woman's Hospital there were 75 hemorrhagic cysts with intraperitoneal bleeding in 7 cases, or 9.3 per

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For lack of space this paper cannot be published in its complete form, but will appear so in the author's reprints.

cent. In a series of 29 ovarian cysts associated with pregnancy, at the New York Lying-In Hospital, confirmed at operation, rupture and intraperitoneal hemorrhage occurred in only one case.

ETIOLOGY AND PATHOGENESIS

Among the host of factors enumerated, a large number concern the origin of ovarian hematoma as well as of intraperitoneal ovarian bleeding, since many cases of the latter are found to be secondary to rupture of a hematoma. On the other hand certain etiologic factors (e. g., adhesions, and sclerosis of the tunica albuginea) tend to impair surface bleeding and at the same time predispose toward hematoma.

* * * *

The causes which act to produce ovarian hemorrhage may be summarized as follows:

I. General Causes Predisposing to Bleeding

1. Acute infections: typhoid, sepsis, acute appendicitis, etc.
2. Acute toxemias: metal poisoning
3. Blood dyscrasias: hemophilia, leucemia
4. Chronic passive congestion: cardiorenal and respiratory disease
5. Hypertension
6. Increased capillary permeability
7. Lowered platelet count
8. Pregnancy
9. Exposure to cold

II. Local Causes

A. In Internal Genital Organs

1. Hyperemia of ovulation, menstruation, pregnancy, and sexual relations
2. Local passive congestion: tumors, pregnancy, torsion of pedicle, malpositions and prolapsus; strains in heavy work, defecation, or sexual excess; postoperative congestion
3. Pelvic inflammatory disease
4. Varicose veins
5. Coexistent tubal pregnancy
6. Trauma: coitus, etc.

B. In Ovary

1. Normal cyclic changes in follicle, corpus luteum and blood vessels
2. Chronic inflammation and sclerosis of parenchyma, tunica albuginea, and blood vessels
3. Interference with follicle maturation, dehiscence and retrogression with consequent cystic degeneration
4. Endometriosis and neoplasm

* * * *

PATHOLOGY

The reported operative, gross and microscopic findings in my 26 cases include most of the nonneoplastic lesions described under ovarian pathology. The effusion is described as thin serosanguineous, fresh bloody, thick tarry or chocolate matter, with or without clots; and its

amount from two tablespoonfuls to over two quarts or "the entire abdomen and pelvis full." The predominating gross finding is a ruptured ovarian cyst (8 times), follicle (3 times), or corpus luteum (eleven times) but in four cases the picture is one of ruptured "chocolate cyst," and in one case that of dermoid cyst, while twisting of the pedicle and rupture occurs in two instances. The appendix is reported normal 14 times, chronically inflamed three times. Inflammation of the adnexa on the side of the bleeding occurs but twice, on both sides once, hydrosalpinx twice, prolapsed adnexa three times. Adhesions are mentioned 5 times, retroversion 3 times, and myoma uteri twice. The chocolate cysts proved to be endometriosis in one case while the others showed the typical pathology of hemorrhagic cyst.

The histologic exclusion of chorionic tissue is theoretically weakened by the failure to serially section the entire ovary (and tubes). In a single instance the hemorrhagic cavity in the ovary was seen to communicate with blood on the peritoneal surface by a narrow channel; and in numerous instances there are found small and large hemorrhages in the ovarian parenchyma subjacent to the surface and even in the tunica albuginea. Microscopic examination of the numerous "hemorrhagic cysts" in the series reveals hemorrhages of all sizes in their walls. These walls are sometimes composed of "nonspecific ovarian stroma," of corpus luteum folds in various stages, of lamellated connective tissue, of granulosa cells or other follicle derivatives; in one instance typical dermoid structures; in another endometrioid tissue. Various disturbances in follicular maturation, microcystic degeneration, connective tissue and leucocytic infiltration, and distortion of stroma and tunica by edema are repeatedly found; and blood vessel changes include great increase in numbers, with their lumen crowded by red cells; or on the other hand sclerosis and hyalinization of their walls with numbers of round cells inside and outside the vessels. The tunica albuginea is by no means uniformly thickened; and the surface epithelium varies from the highest cylindrical to low cuboidal or flat cells, in one case with pseudofollicular inclusions in both tube and ovary. In no case are fetal elements noted; and nothing like cavernous or angiomatous formations occur in the series studied. Beside the chronic productive changes noted there was evidence of ovarian inflammation in a polymorphonuclear infiltration in one case; and the tubes were chronically inflamed in four instances.

The above findings obviously do not satisfy Forssner's first criterion since pregnancy in tube or ovary is not excluded by serial sections; and his third criterion, pathologic alteration in the ovary of sufficient gravity to predispose to severe hemorrhage, is not much better satisfied except in the case with torsion of the pedicle and massive congestion of the ovary. Nevertheless, they do exemplify the multiplicity of changes, anatomical and functional, cyclic and noncyclic; physiologic and pathologic, sudden and gradual, to which the ovary must submit. That these

changes are sometimes accompanied by lesions outside the ovary is self-evident from reports in the literature of ovarian hemorrhage.

* * * *

SYMPTOMS

The clinical grouping of Guyot and Villar is applicable regardless of the pathology present: (1) massive hemorrhage; (2) discrete hemorrhage with signs of peritoneal irritation; (3) hematocele of ovarian origin. In general, these varieties parallel those of ruptured tubal gestation; but the large number of cases with other coexistent pathology inside and outside the ovary, present confusing clinical pictures so that the ovarian hemorrhage is not suspected. Study of the clinical history and physical signs in these cases shows that the history is of chief value in determining the true origin of the hemorrhage. Among the most important of these are the following:

* * * *

Relation of Onset of Pain to Ovulation and Menstruation.—Not noted in 5 cases, unrelated in 6 cases, leaves 15 of the series in which the onset of the pain was related to the last period, as follows:

Pain before last period in 3 cases, 20 per cent (three days, two days, seven days premenstrual).

Pain with last period in 3 cases, 20 per cent (first day, second day, Case XVIII on first day after nine weeks of amenorrhea).

Pain after last period in 6 cases, 40 per cent. Onset on thirteenth to sixteenth day, corresponding to ovulation time.

Of the remaining 3 cases, Case XXVI occurred five weeks after last period in a patient with a thirty-five-day cycle, estimated to be two days overdue. In other words pain occurred at time of "suppressed menstruation." Case XVII followed one day after cessation of the last period which was thought to be one week early; Case VI began as the menses ceased on the fourth day.

From this it is apparent that these 15 cases have the onset of pain closely related either to ovulation in 40 per cent or to the premenstrual and menstrual period in 60 per cent. In other words the first and second weeks after menstrual period seem excluded from the clinical picture of ovarian hemorrhage. The 6 nonrelated cases all had chronic or dull pain over long periods of time. The literature yields the following views: Bovée states that the largest number occur during or close to the period. Relatively few (Bürger, Sudeck, Barolin Case III) occur actually at menstruation, although in Lindig's and Winiwarter's cases the onset was at the estimated due-date of the period but the latter was delayed. The majority of cases began in the premenstrual period (Adams, Luker, Urban, Lockyer, and Benthin). Pankow's case occurred at estimated ovulation time. Simon sums up this relationship thus: The great majority occur in the second to fourth week of the cycle, i.e., from the time of ovulation to menstruation, and this holds for both the massive and discrete hemorrhages.

* * * *

PHYSICAL SIGNS

The general appearance varies from normal, through stages of anxiety and suffering to pallor, prostration, and collapse. The temperature usually 98.6° on admission, pulse varies from 75 to 112, usually good quality. The blood pressure was on average levels. Nothing unusual noted in head, neck and chest, breasts, extremities, and reflexes. The

abdomen usually is symmetric, distended in 2 cases, tender over the lower half in 1, the right lower quadrant in 11, the left lower quadrant in 6, McBurney's region in 5, epigastrium in 1 case. Rigidity noted in 12 cases. Shifting dullness and other signs of fluid are reported in Olsen's case (950 c.c. of blood recovered at operation), not noted in the present series. Pelvic examination is often confusing on account of other coexistent pathology. Intact hymen will often limit the examination to the rectum. The absence of bleeding is noteworthy as is the absence of any softening of cervix, Hegar sign, or uterine enlargement. There were two 3° retroversions and tenderness on motion in 4 cases. The adnexa were tender on one side 9 times, and once on both sides; enlarged or cystic 10 times including bilateral enlargement in 2 cases. A vague fullness in the right fornix was noted in two cases; while in only one case was tenderness in the culdesac reported.

Vaginal puncture not done. Wassermann negative. Aschheim-Zondek test was done once with negative result. Hemoglobin and erythrocyte counts: normal in all but two cases: 75 per cent with R.B.C. 3,950,000 in Case XVII with effusion of one pint of blood; 55 per cent with 2,096,000 in Case XXIII with "abdomen full of fresh blood and clots."

Leucocytes averaged 13,000 in 21 cases with extremes 7,200 and 22,900. Polymorphonuclears average 76.8 per cent, extremes 60 to 92 per cent. Farrar's contention that the leucocytosis is due to peritoneal irritation from extravasated blood rather than to tissue destruction, is borne out by two cases of hemorrhage with high white count reported by Danforth, one from aneurysm of the splenic artery and the other from rupture of the inferior mesenteric vein.

Sedimentation tests in 4 cases averaged 13 mm. for the first hour. In three of these cases, ectopic pregnancy was considered.

Preoperative diagnosis in 25 cases included appendicitis 14 times (8 acute, 3 subacute); ovarian cyst 4 times; ectopic 4 times; ectopic or adnexal disease twice; and acute surgical abdomen due to perforated ulcer or appendix, once. Certainly the physical signs include nothing peculiar to ovarian hemorrhage, pointing merely to peritoneal irritation, to internal hemorrhage or disease of the pelvic organs. The utter dependence upon the clinical history becomes evident.

DIFFERENTIAL DIAGNOSIS

Diagnosis is rendered difficult by the coexistence of various pelvic diseases with the hemorrhage. Discrete hemorrhages are most often mistaken for appendicitis, and by no means is the mistake limited to right-sided ovarian hemorrhage. The pain of appendicitis often grows worse whether or not an interval of respite occurs. In ovarian hemorrhage the pain is very sudden and agonizing and often shows steady recession and disappearance. Pain occurring during the first two weeks after menstruation points away from an ovarian origin. The absence of temperature elevation, and the rapid fall of the leucocyte count and sedimentation rate, argue for extravasated blood rather than for infection. Hence the importance of frequently repeated white counts and sedimentation tests.

The latter points will usually serve also to differentiate inflammatory disease of the adnexa. On the other hand, great difficulty may be had in

those cases with epigastric pain and rigidity, to rule out cholecystitis and perforated peptic ulcer. The history is of paramount importance; while resort to vaginal puncture may *not* clear up the diagnosis, since both ovarian hematoma and tubal pregnancy may be unruptured.

Massive hemorrhage in the young woman will usually be diagnosed as due to ruptured ectopic pregnancy, a mistake of medicolegal rather than clinical importance, since the treatment is in any case operative. Absence of amenorrhea, absence of metorrhagia, absence of presumptive signs and symptoms of pregnancy and absence of the premonitory lancinating unilateral pain of unruptured ectopic, but a history of previous attacks of pain like the present illness, social status precluding legitimate pregnancy, absence of previous pelvic disease or sterility, absence of uterine enlargement and decidual reaction (diagnostic curettage), all point to internal hemorrhage *not* due to pregnancy. On the other hand, a tubal abortion with the syndrome of pain, shock and recovery will be impossible to differentiate, unless the history makes it improbable. The cases studied at Woman's Hospital include mistakes in both directions: Case 44286 operated by Byron Goff appeared at operation to be a ruptured follicle, only upon histologic examination was ovarian pregnancy determined. Case 42162 was discharged without operation with the diagnosis of "ruptured corpus luteum," only to return three weeks later when the ruptured ectopic gestation was confirmed at operation. Numerous cases of chocolate cyst have revealed chorionic tissue at histologic examination; and the reverse occasionally appears. Bissell operated under the diagnosis of bilateral ectopic pregnancy; and active bleeding was demonstrated both from a ruptured corpus luteum on one side and from a tubal pregnancy on the other. Reference has been made to Waters' case of intra-cystic hemorrhage with the clinical picture of unruptured ectopic. The hormone test may be used in cases that are not too urgent, but a negative result is of little value. Finally, mention may be made of the following reported causes of hemoperitoneum: (1) traumatic rupture of a viscus or mesentery, (2) ruptured aneurysm, (3) rupture of a varicose vein of the broad ligament, or of the pregnant uterus, or of a subserous myoma, (4) reflex uterine bleeding due to an obstructing submucous myoma or to atresia of the genital canal, (5) perforating chorionepithelioma of uterus or tubes (Anspach and Hoffmann; Creysel and Boyer), (6) rupture of the pregnant uterus after cesarean section or myomectomy. Most of these conditions are improbable in the healthy, young nulliparous woman subject to ovarian hemorrhage.

PROGNOSIS

Death from internal hemorrhage was fairly frequent in the days when extrauterine pregnancy was not treated by laparotomy; it is the exception in the untreated ovarian hemorrhage although the literature contains a number of such deaths confirmed by autopsy. Hedde found only 15 cases up to 1913 in which ovarian hemorrhage was dangerous to life.

In the operated cases without complications, recovery follows in practically 100 per cent; and the same is true of the milder cases without intervention. There was no death in Simon's 30 operated cases of corpus luteum hemorrhage, in 14 of which the hemorrhage varied from one-half to more than one liter, while the other 16 cases showed 50 c.c. of blood or less. In the present heterogeneous group of 26 cases there was no death.

Recurrences have been repeatedly verified; and Jayle believes the lesion tends to be bilateral. Of the present series, 18 cases have been followed from one month to three years with recurrence of pain in two cases: one of these is a slight discomfort in the right lower quadrant; the other had several attacks entirely similar to previous attack and leading to the suspicion of "acute abdomen." These attacks subsided under morphine and rest. In six, menstrual disorders have been relieved by the operation; in one case menopausal symptoms have been induced. Case 3 has been operated three years after first operation, and the diagnosis of ruptured ectopic gestation confirmed pathologically. Two patients have had normal labors, a third has had a miscarriage. An interesting immediate result, often reported hitherto, is a red vaginal discharge for one to several of the first ten postoperative days, noted in ten of the 26 histories. Ovarian hemorrhage, even of small size, may be a potent cause of adnexal adhesions found in young girls with no pelvic disease (Gersuny). During the five years, 1926 to 1930, at Woman's Hospital, 46 cases were discharged without operation and with the diagnosis of cyst of ovary, of which 8 were thought to be corpus luteum cysts. One of these returned within a month for operation when ectopic pregnancy was confirmed at operation.

PROPHYLAXIS AND TREATMENT

Normal habits and avoidance of predisposing general and pelvic diseases, as well as the exciting causes such as trauma, exposure to cold at menstrual periods, overexcitement, or physical overstrain seem the best safeguards. Proper treatment of menstrual disorders and malpositions are indicated as well as care in pelvic examination and operative handling. Relief of retroversion and prolapsed adnexa may eliminate passive hyperemia and direct trauma per vaginam. Removal of ovarian cysts, even if small, should be practiced routinely.

Treatment of ovarian hemorrhage in the massive effusions, calls for laparotomy and control of the bleeding. This may necessitate oophorectomy; but usually a wedge-resection or a simple mattress suturing of the ovary will suffice. Bilateral oophorectomy, once recommended by Jayle and Primrose, is never justified for this condition alone. Schumann decries the policy of watchful waiting in ectopic hemorrhage; but many surgeons advocate a preliminary period of observation and supportive treatment, controlled by frequent white blood counts and blood pressure readings. In the smaller or discrete ovarian hemorrhages, delay will

certainly obviate some operations and some mistakes in diagnosis, especially where there is time for one of the hormone tests of pregnancy. Where confusion exists with acute appendicitis, attention to Turner's recent caution will justify the occasional needless operation. He states that appendicitis is still extremely serious, causing 1.2 per cent of the deaths from all causes in this country in 1926. As for the cases that have reached the stage of hematocele, one may recall the counsel of Fritsch: *noli me tangere* unless secondary suppuration and pointing supervene. Naturally in the mixed group of cases here reported, operation was often directed primarily at the diseased pelvic organs, the cure of intraperitoneal hemorrhage being incidental.

CONCLUSIONS

1. In 21 out of 26 cases of intraperitoneal hemorrhage of ovarian origin, the symptoms are related to the bleeding ovary. In 5 cases (19.2 per cent) the other pelvic pathology entirely overshadows the bleeding.

2. Microcystic degeneration as a cause of ovarian hemorrhage is not sustained, although both conditions may be manifestations of a disturbance in the growth, maturation, rupture, and metamorphosis of the follicle.

3. The wide variety of normal and pathologic alterations of the ovary is shown by this series. In the light of these factors, trauma seems only to hasten or aggravate a condition already destined to occur.

4. Correlation between menstrual history, onset of symptoms, and the cyclic stage of the removed ovarian and endometrial tissue should in the future add to our knowledge of the pathogenesis and diagnosis of the condition.

5. Massive ovarian hemorrhage will be mistaken by careful observers for ruptured extrauterine pregnancy unless due weight and credence are given to the clinical history and social status of the patient. The attendant should refrain, wherever the social status of the patient precludes legitimate pregnancy, from making the diagnosis of "ectopic" until it is proved by pathologic examination.

6. Discrete ovarian hemorrhage will be mistaken for acute and subsiding acute appendicitis and lead to unnecessary operation. If the onset of pain be correlated to the estimated ovulation-time as well as to the date of menstruation, and if this relation applies to the previous attacks, one may suspect the ovary; and a rapid fall in white and poly counts and sedimentation rate points to cessation of bleeding as well as absorption of the effused blood.

7. The occurrence of ovarian hemorrhage due to trauma per vaginam adds another to the classical indications for the correction of retroversion and ovarian prolapse.

8. Two things are needed to bring these cases to light: first, report of these excusable mistakes in diagnosis; and second, an index-heading,

"Hemoperitoneum" under which all intraabdominal hemorrhage cases, whatever the cause and severity, can be filed.

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120 EAST SEVENTY-FIFTH STREET

(For discussion, see page 908.)

THE INVESTIGATION OF STERILITY*†

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STERILITY is one of the most important problems facing the gynecologist. A complete study of the subject is possible only in a well organized clinic which includes a personnel equipped to carry out investigations dealing with its many phases.

The efforts of Hühner,¹ Cary,² Moench,³ and others have properly placed the responsibility for a high percentage of sterile matings upon the shoulders of the husband. We agree with Meaker⁴ upon the necessity for thorough medical study of both husband and wife, and upon the importance of seeking multiple etiologic factors in the investigation of each sterile marriage.

History.—A careful history of both husband and wife, taken at separate sittings, will often give leads into proper channels for further investigation. In the marital history, the question of previous marriages and pregnancies arises. Contraception, practised for a number of years, is said by Rubin⁵ to be a factor in the production of sterility. In the present marriage, if there have been pregnancies, a detailed discussion of the terminations, with particular attention to the possibility of post-partum infection, is in order.

*Read at a meeting of the Obstetrical Society of Philadelphia, October 1, 1931.

†For lack of space, it is not possible to include here the special record sheets used in this Clinic, but copies of these may be secured on application to the authors.

Valuable information is at times obtained from the developmental and past medical history. The age of puberty, the development of the skeletal framework, the onset and character of the menses, and the history of illness during adolescence are important points. Meaker⁶ emphasizes developmental arrest in the female as the result of transient glandular insufficiency during puberty. Such arrest is suspected from the history of abnormal menstrual onset or the presence of some constitutional debility at that time. It may leave permanent hypoplasia of the pelvic organs with accompanying menstrual aberrations and sterility.

The history of previous attacks suggestive of pelvic inflammation is occasionally obtained. Minor infections may complicate dilatation and curettage for dysmenorrhea or sterility and, through tubal occlusion, seal the fates of would-be mothers. The possibility of infection following artificial insemination or repeated insufflations improperly done is to be considered. Nonspecific postpartal infections are frequently more easily diagnosed from the history than from the pelvic examination. The induced abortion of the first and undesired pregnancy is a leader among the causes of occluded fallopian tubes. A history of acute appendicitis with operation and drainage should arouse suspicion of perisalpingitis and peri-oophoritis. Discussion of the family history consists of questions as to the fertility of the parents, brothers, and sisters, and the presence of any familial endocrinal disorders.

In the past history of the husband, particular attention is paid to venereal infections, mumps, orchitis or evidence of former genital tuberculosis. Conditions adjacent to the spermatie passages, such as, hernia, hydrocele, and varicocele have little etiologic importance except for the possibility of injury to the spermatie channels at operation. The habits and occupation of the male are scrutinized. Alcoholic or narcotic addiction impair spermatie vigor; workers with lead, phosphorus, or x-rays may be similarly affected.

The sex lives of the individuals must be tactfully investigated. Frigidity, while not an absolute bar, is a restraining influence. It has been shown that sexual excess definitely reduces fertility.

Important points in the present status of the patients are the general health, marked loss or gain in weight and extreme fatigue. Nervous exhaustion in the male may reduce spermatie potency. The menstrual habits are discussed in detail. The presence of amenorrhea, dysmenorrhea, menorrhagia or metrorrhagia may indicate a local or constitutional disturbance resulting in sterility. Full information concerning diet is significant. It is now proved, both experimentally and clinically, that dietary deficiencies result in lowered fertility in both male and female. Macomber⁷ has stressed the importance of diets well balanced in protein, fat, and carbohydrate, as well as vitamin and mineral salt content. A large percentage of sterility patients studied by him showed some form of dietary deficiency.

Physical Examination.—Valuable information may be obtained from the general physical examination of both husband and wife. Particular attention is given to evidence of endocrinal unbalance, constitutional defects and foci of infection. Careful study of the teeth and throat is necessary. Foci here may play a definite rôle in depressed states which lower fertility. In addition to these studies the husband is referred for a genitourinary examination. The ordinary male defects, except testicular aplasia, are unimportant. Inflammatory conditions, involving the epididymis or testicle may produce sterility.

In the routine pelvic examination, evidence of congenital defects, infection, and endocrinal malfunction are sought. Pelvic hypoplasia is now considered to be but local evidence of past or present glandular derangement. The character of the bony pelvis, whether normally feminine with small bones or funnel-shaped (pseudo-masculine) with thick, heavy bones is noted. In many hypoplastic cases the pelvic bones retain their juvenile proportions. The vulva and introitus are carefully inspected. Bartholin's and Skene's glands are examined for evidence of infection. The vaginal pool and chemical reaction are now considered less important than formerly. We agree with Hühner,⁸ Meaker,⁹ and Moench¹⁰ that the alkalinity of the semen and cervical secretion is sufficient to counteract the average vaginal acidity. The use of the precoital bicarbonate douche is not recommended in our clinic because of the likelihood of too great alkalinity. The fertilizing sperm is probably deposited at the external cervical os, and does not ascend from the so-called vaginal pool. The cervico-uterine proportion, in the absence of infection with hypertrophy, is of value in diagnosing hypoplasia. With the normal proportion of the cervix to the uterus, as 1 is to 2, the reverse is frequently seen in severe endocrinal aberrations, with gradations between the two in less marked cases. Of great importance is the viscosity of the endocervical mucus, particularly in the presence of the pin point os. In chronic endocervicitis, an important factor in the production of sterility is the tenacious mucus plug which offers a bar to spermatie ascent.

The condition of the uterine body is noted. Retrodisplacement does not preclude pregnancy, but may reduce its probability. Antelexion is usually to be considered a normal finding, but occasionally it forms part of an endocrinal picture, and under either circumstance the flexion per se is rarely a factor in sterility.

The adnexa are palpated for evidence of inflammatory disease. Multiple small follicular cysts of the ovaries are frequently associated with menstrual disturbances and sterility. The history and clinical picture are of more value in diagnosing this condition than the pelvic examination, since it often escapes detection by palpation.

Special Gynecologic Examination.—In our clinic the study of the male semen is done by the gynecologist. The postcoital examination was popularized by Hühner⁸ in 1913 and usually bears his name. This test is im-

portant and is the first specialized study made. Theoretic doubt has recently been cast upon its dependability by Moench,¹¹ who claims that an hour following intercourse the fertilizing sperm is probably well up the cervical canal. However, it is of value, when used in conjunction with routine examination of the sheath specimen. This consists first of estimation of the amount, viscosity and reaction of the semen. Cary believes that repeated small ejaculates indicate lowered fertility. This may be the result of too frequent coitus. Estimation of the number of spermatozoa is made in a manner similar to that of the ordinary blood count. The normal number is 100 to 150 million sperms per cubic centimeter. A count of less than 100,000 per c.c. indicates clinical sterility. A warm stage mount is examined for the relative number, endurance, and motility of the sperms, and for the presence of pus cells. Finally a stained smear is studied for abnormal forms. Moench¹² claims that abnormal sperm heads furnish the best index to their fitness for reproduction. According to him, 25 per cent abnormal heads indicates clinical male sterility.

Patency Tests.—Of the two popular tests for the patency of the fallopian tubes, we prefer insufflation for routine work, and utilize the Rubin apparatus with the kymographic attachment. The graphic record is of great value in detailed diagnosis of tubal pathology and in recording the results of repeated insufflations. Should doubt arise as to whether or not gas has passed through the tubes, fluoroscopic demonstration of the CO₂ lemniscus under the diaphragm is employed. This test should be a routine procedure in the study of every sterility problem, without obvious cause, if none of the contraindications are encountered.

Our experience with the use of lipiodol has been limited. In cases of complete tubal obstruction, diagnosed and confirmed by repeated insufflation, we attempt to localize the obstruction by lipiodol injection.

Laboratory Investigation.—Routine examination of the blood and urine is indicated. Moderate to marked anemia is a definite factor in reduced fertility in both sexes. A serologic examination is made although the presence of syphilis is not as great a factor in the production of infertility as it is in miscarriages and premature stillbirths.

If no absolute impediment to fertility has been discovered, the study proceeds into the field of endocrinology. Remarkable advances have recently been made in gynecologic endocrinology, and we are on the threshold of more startling developments, particularly in organotherapy.

Dysfunction of the thyroid gland, as evidenced by clinical signs and basal metabolic disturbances in both male and female, is known to reduce fertility. Endocrinologists state that it is better to take the average of several basal metabolic determinations, particularly when subnormal function is suspected. In the absence of subnormal estimations, with clinical evidence of lowered thyroid activity, cautious treatment along these lines is recommended. This is the only type of organotherapy which at present is recognized as being clinically effective.

Efforts to ascertain pituitary dysfunction are directed along several lines. The most dependable evidence lies in various physical stigmas; faulty skeletal development, abnormal fat and hair distribution, pelvic hypoplasia and various eye changes. The latter facts are obtained from ophthalmologic examination in which, as Mazer¹³ indicated, contraction of the visual fields, enlargement of the blind spot, and increased yellow color of the discs point to pituitary dysfunction. X-ray study of the long bones, skull, and sella turcica are of occasional value. The glucose tolerance test is routinely done because of the increased tolerance for sugars seen in posterior pituitary disease which is frequently associated with dysfunction of the anterior lobe. Blood and urine hormone studies in pituitary investigation are valueless. In the absence of pregnancy, no test is yet devised to detect the normal amount of pituitary hormone in the blood or urine.

In ovarian hypofunction, however, the female sex hormone and the pituitary hormone tests are of value. The Frank¹⁴ test is based upon the action of the female sex hormone upon the lower generative tract of the spayed mouse, namely, the induction of estrus. Frank has demonstrated that in normal, fertile women there is a definite premenstrual increase in the female sex hormone of the blood. In various menstrual irregularities such premenstrual increase does not occur. Likewise, in many women with functional sterility who menstruate regularly, there is no premenstrual increase in the female sex hormone. Hence in regularly menstruating, functionally sterile women, a Frank test, showing no premenstrual wave, is indicative of hypoovarian function.

Confirmation of this is often found in the pituitary hormone test recommended by Fluhmann.¹⁵ This test, a modification of the pregnancy test of Aschheim and Zondek, utilizes the action of the anterior pituitary hormone upon the ovaries of immature mice. Fluhmann and others have demonstrated that in human castrates, from radium, surgery, or spontaneous menopause, there is a compensatory increase of the anterior pituitary function, with more hormone in the blood. Likewise, in sterile or certain amenorrheic subjects with apparent reduction in ovarian function, a definite increase in the pituitary hormone may be demonstrated in the blood, similar to but less marked than that seen in pregnancy. Therefore, in those patients with decreased follicular hormone, as evidenced by the Frank test, and increased pituitary hormone as determined by the Fluhmann test, one may be justified in making a diagnosis of primary ovarian secretory failure. In the other group, presenting no increase in pituitary hormone, the ovarian failure is probably secondary to pituitary dysfunction.

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133 SOUTH THIRTY-SIXTH STREET.

(For discussion, see page 914.)

NUPERCAIN IN SPINAL ANESTHESIA

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THE principles of administration of novocain and the advantages of its use in intraspinal block anesthesia for operations below the diaphragm need no reiteration.

On March 21, 1931, the Council of Pharmacy and Chemistry of the American Medical Association accepted a new anesthetic agent, Nupercain or Percain, synthesized from the quinine nucleus, chemically known as alpha-butyloxyinchonic acid diethylethylene-diamide hydrochloride. For use in spinal anesthesia, it is dispensed in 2 c.c. ampules of a 1:200 dilution in physiologic saline, acidified by one drop of concentrated hydrochloric acid per liter of solution. In this dilution its effects are nontoxic, although pharmacologically it is five times as toxic as cocain when injected intravenously into rabbits and twice as toxic when injected intravenously into dogs.

Satisfactory spinal anesthesia lasting from three to ten hours has been reported by Keyes³ in a series of 46 cases and by Zieger⁴ in a series of 52 cases.

ACTION OF NUPERCAIN

Nupercain has a specific chemical affinity for nerve fibers as does novocain but to a slightly less degree. There is less effect on the sympathetic fibers in the anterior roots which control vasoconstrictor action on the great splanchnic bed of blood vessels. For this reason we have proportionately less fall in blood pressure and maintenance at a more constant level as will be shown later. The decreased toxic action of nupercain is not due to less toxicity of the drug, for this is known to be greater, but to its greater dilution which makes rapid absorption of large amounts impossible.

The serious effect of spinal block is due to the cerebral anemia initiated by the sympathetic paralysis which permits pooling of the blood in the visceral area and in any dependent portion of the body. It is therefore important in using nupercain to counteract splanchnic vasodilatation and blood pressure fall by means of ephedrine, and cerebral anemia by use of the Trendelenburg position.

FACTORS CONTROLLING HEIGHT OF ANESTHESIA WITH NUPERCAIN

It has been shown by a number of investigators that there is no active circulation of the spinal fluid. Therefore the diffusion of substances introduced into the spinal canal is dependent upon the laws of diffusion of one fluid in another within a closed vessel. With novocain crystals dissolved in spinal fluid, the anesthetic mixture has a specific gravity in excess of the normal for spinal fluid of 1005. However, this difference is so small that for practical purposes the chief factor in obtaining height of anesthesia is the amount of spinal fluid withdrawn and reinjected.

Several workers have employed solutions of lighter or heavier specific gravity than that of the spinal fluid, combining with this, posture of the patient to obtain various levels of anesthesia. Pitkin for example introduced such solutions with the claim of increased duration of anesthesia and greater accuracy in placing its level. Spinocain acts as a floating solution while intact but quickly diffuses in the spinal fluid. Novocain, the principal constituent, gravitates, giving primarily a posterior root effect. Although I have followed Pitkin's technic carefully, I have never been able to duplicate his results. My experience has shown delayed anesthesia with predominant posterior root effect, no constant increase in duration, and much greater fall in blood pressure. The latter I am sure is due to a fallacy in the Pitkin technic in which ephedrine is given at the time of lumbar puncture, permitting vasomotor paralysis before a well-sustained ephedrine action can be established. It is important that ephedrine be administered at least ten minutes before administration of the anesthesia.

To obtain various levels of anesthesia with nupercain, the same principle of volume control used with novocain crystals has been employed. The capacity of the spinal canal from the sixth thoracic vertebra to the lower lumbar region is about 8 c.c. The proper amount of novocain dissolved in the withdrawn 8 c.c. of spinal fluid, and reinjected in the second lumbar space will therefore produce anesthesia to the nipple line. Other levels may be accurately obtained by similar injections of varying amounts of the novocain spinal fluid mixture. The above principle is employed with nupercain.

The difference in specific gravity between nupercain in physiologic salt solution and the normal spinal fluid is extremely slight. Novocain mixtures with spinal fluid are definitely of greater specific gravity than is the spinal fluid. A knowledge of these differences in the two solutions is important in comparing and explaining the difference in their anesthetic action. Prompt anesthesia results from novocain because the hyperbaric solution of novocain immediately settles around the posterior roots in the dorsal decubitus position while the isobaric or perhaps hypobaric nupercain solution permits slower contact or establishes anterior

root block first. Jones² therefore suggests that in administering nupercain, the patient be placed in the ventral decubitus position for a few minutes following administration in order to saturate the posterior roots, then returned to the dorsal position to obtain anesthesia of the anterior roots. This procedure will give quicker and more uniform anesthesia.

DURATION OF ANESTHESIA

Anesthesia of approximately one hour's duration is obtained by the use of from 120 to 150 mg. of novocain. Larger amounts of novocain will produce longer periods of anesthesia, but the danger line between the balancing effect of increased doses of ephedrine and the larger amounts of novocain may be reached with undesirable and even serious symptoms following large drops in systolic blood pressure. With nupercain, surgical anesthesia for three to five hours may be obtained with no increase in dosage and with less systemic reaction than with the average dose of novocain. It therefore has a distinct place in regional block in which lengthened anesthesia is required.

A high carbohydrate, nonresidue diet is given the evening before operation and fluids forced to the limit. Although it has not been proved that the barbital derivatives produce the same specific protective action against nupercain as against novocain poisoning, sodium amytal gr. iii or Nembutal gr. iii are used as a sedative the night before and the dose repeated one and a half hours before operation the following morning. In most cases a decided hypnotic result is obtained from this dosage so that the trip to the operating room is only a dim memory. In addition one-sixth or one-quarter grain of morphine sulphate is given hypodermically forty-five minutes before operation and 50 to 100 mg. of ephedrine administered by hypodermic just before the patient leaves his room. In this way a well established vasoconstrictor action may be obtained before the anesthetic mixture is introduced. A small gauge spinal needle is used for the puncture, which is always done with the patient on one side, the Trendelenburg position being instituted immediately on completion of the administration of the anesthetic. Throughout the administration of the anesthetic the patient's condition is carefully observed and blood pressure readings taken. In case the patient complains of any discomfort, real or imaginary, light gas anesthesia is immediately instituted. This I feel is an important point in the conduct of the case, and one of which many surgeons do not avail themselves. In this way, the patient experiences no physical or psychic shock and the surgeon still has all the advantages of the spinal block anesthesia for his work.

Upon his return to bed the patient is kept in the prone position for twenty-four hours to prevent possible postanesthetic headache. Liquids both for food and fluid intake are started immediately.

ANALYSIS OF RESULTS

A series of 45 cases, personally anesthetized and operated upon, prepared as outlined above, are included in this study. Of this number 20 per cent consisted of operations in the upper abdomen and 80 per cent in the lower abdomen. Of the lower abdominal operations nearly 27 per cent were combined abdominal and perineal gynecologic operations.

Nearly 6 per cent of cases showed some postanesthetic headache as compared with 1.9 per cent in a series of 151 cases previously reported¹ in which novocain was administered. There was a definitely increased incidence of postanesthetic headache following the use of nupercain, although none were severe or of more than twenty-four hours' duration.

No failures were experienced in the cases in which the anesthetic was administered personally. In two cases not included in this series in which the anesthetic was given by interns learning the technic, the results were not satisfactory. If no anesthesia follows the use of nupercain, I feel certain that there has been some error in the technic of administration as in the case of failure following the use of novocain. If the nerve roots are bathed with either solution, anesthesia is assured.

Two patients of this series were given 3 c.c. of nupercain without ill effects or additional advantage in anesthesia; the remainder of the series received 2 c.c. of nupercain.

As will be noted in Table I, greater fall in blood pressure occurred in cases of upper abdominal surgery. Larger doses of ephedrine (100 mg.) are therefore indicated in this type of case. No advantage from larger dosage was derived in the cases of pelvic surgery.

TABLE I

	AVERAGE RISE IN SYSTOLIC BLOOD PRESSURE	PER CENT CASES	AVERAGE DROP IN SYSTOLIC BLOOD PRESSURE	PER CENT CASES
Upper Abdominal Cases	12.5 mm.	4.5	22.2 mm.	24.5
Lower Abdominal and perineal	14.3 mm.	15.5	12.5 mm.	55.5
Total all cases	13.4 mm.	20.0	17.3 mm.	80.0

Personal susceptibility to nupercain is a negligible factor, the only reaction to the anesthetic being occasional slight nausea. Nervousness on the part of three patients was overcome by the use of a light gas anesthesia.

All spinal punctures were made in the second lumbar space. For lower abdominal operations from 4 to 5 c.c. of spinal fluid was withdrawn, 2 c.c. of which were discarded and replaced by 2 c.c. of the nupercain solution. In upper abdominal operations 7 to 8 c.c. of spinal fluid

was withdrawn and 2 c.c. replaced by the nupercain. No advantage was observed by the addition of the 2 c.c. of nupercain to the total amount of spinal fluid withdrawn with reinjection of the mixture under this additional pressure, although it would seem that this procedure would tend to increase absorption and result in quicker and more uniform anesthesia.

The time required for the onset of surgical anesthesia with nupercain is from eight to fifteen minutes. It is important to remember this point in the use of nupercain as compared with novocain, as with novocain sufficient anesthesia is obtained almost instantly. This seeming delay is not a disadvantage, however, as some time must be consumed in preparing and draping the patient.

Table I shows the average increase and decrease of the systolic blood pressure. Keyes³ reports an average fall of 18 mm. in all his cases, which corresponds almost exactly with the figure of 17.3 mm. for this series. He compared this fall in blood pressure with that of 31 mm. following the use of novocain crystals and 39 mm. following the use of spinocain. He called attention particularly to the decreased but abrupt fall in blood pressure following the use of nupercain, with a constant maintenance of the low level until the pressure gradually returns to normal. With the use of novocain and spinocain the original decline is more gradual, the lowest point being reached in about one-half hour.

The action of nupercain on sympathetic fibers as typified by the graphic blood pressure curves has a distinct advantage over the action of novocain, in that we do not have to anticipate additional fall in systolic blood pressure as the anesthesia progresses. Therefore there is no late nausea and vomiting as occasionally occurs with novocain, to disturb the operative procedure.

The duration of anesthesia obtained with the use of nupercain is its chief recommendation. Much of the trouble experienced with the use of procain has come from the necessity of increasing doses in order to increase the duration of anesthesia. With the average safe dosage of nupercain, surgical anesthesia is obtained for one and a half to five hours with an average of about three and one-half hours. Partial anesthesia was observed up to seven and eight hours after operation. This feature of lengthened analgesia contributes in no small way to the comfort of the patient in the immediate postoperative period, especially if morphine and sodium amytal are given before the anesthetic effect of the nupercain is allowed to wear off completely.

CONCLUSION

1. Nupercain is a safe and satisfactory agent for spinal anesthesia when used for operations below the diaphragm.
2. It has the following disadvantages as compared with procain crystals: (a) Lengthened period of onset of anesthesia following ad-

ministration, and (b) definitely greater tendency to postanesthetic headache.

3. It has the following advantages as compared with procain crystals: (a) Less variation in individual susceptibility to the drug; (b) less nausea, vomiting and subjective symptoms because of the better sustained blood pressure level; (c) less blood pressure fall and a more constant level after the initial drop; (d) sufficient length of anesthesia with the average nontoxic dose for all operative procedures, the markedly lengthened analgesia promoting greater immediate postoperative comfort for the patient.

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1109 MEDICO-DENTAL BUILDING.

THE USE OF SODIUM ISOAMYLETHYLBARBITURATE (SODIUM AMYTAL) IN THE TREATMENT OF ECLAMPSIA*

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FOR the past year we have employed sodium amytal in the treatment of eclamptic patients, at the Charity Hospital with results so gratifying that we feel that a preliminary report is justified. Two important points are to be observed when it is exhibited by the intravenous route. First, no solution should be used which is not absolutely clear for four or five minutes after its preparation. Second, the rate of administration of the solution should not exceed 1 c.c. per minute. The effects of the drug are obtained almost immediately, the patient as a rule dropping off into what is apparently a normal sleep after 3 to 6 gr. have been injected.

Several phenomena are noted, following the administration of this preparation. The most marked effect is the rapid lowering of the blood pressure, but this drop apparently has no untoward effect, and the pressure soon rises again, but not to the original level. The most marked fall in our series was one of 96 mm. systolic, from 216 to 126. In another instance, a fall of the systolic pressure from 145 to 70 in five minutes was noted, with a rapid reactionary rise to 100. The respiratory rate is usually decreased, but not, as a rule, to a marked extent. In one patient there was a transient fall to nine per minute. There is generally a slight rise in the pulse rate.

Our report covers a series of 30 cases of ante- and intrapartum eclampsia treated by us in the wards of the Charity Hospital during the past year. A few recently admitted patients are not included. Almost as

many patients suffering from postpartum eclampsia have been cared for, but for various reasons we decided not to consider them in detail in this paper. All of them recovered. The essential feature of the treatment employed was the use of sodium amytal, but other measures were employed as adjuvants.

Of the 30 patients, 20 were colored and 10 were white. Their ages varied from fifteen to forty-one years; 12 were under twenty. The majority were primiparae. The number of convulsions prior to the institution of treatment varied from one to a maximum of 12; 10 women had 4 or more seizures. Only 2 patients had convulsions after the first dose of sodium amytal; one developed one seizure shortly after the injection, the other had 2. The systolic blood pressure ranged from 130 to 240 on admission, in 9 instances it was 200 or over. Albuminuria in varying degrees was a constant finding. Ten patients had a total nonprotein nitrogen in the blood of 40 or more. The blood sugar in the majority of cases was below 100; in 10 patients it was below 80, being reduced to 43 in one instance. Only twice was it found to be over 100, the readings being 114 and 117, respectively. These determinations were, as a rule, made shortly after the admission of the patient; we can not state just when the specimens were taken with reference to the convulsions. Four patients had marked pulmonary edema; 3 of them recovered. Nineteen of the 30 women were at or near term, in the other 11 the pregnancies were between the sixth and eighth months.

Twenty-seven of the 30 mothers recovered. The details of the 3 fatal cases are as follows:

CASE 1.—A white multipara had 4 convulsions before beginning treatment, none after treatment was instituted. Labor was induced by catheter thirty-three hours later. She died on the fourth day in coma. This death, we feel, was due solely to the toxemia.

CASE 2.—This was a colored woman, who had recovered from the eclamptic attack, delivering spontaneously twenty-one hours after admission. No anesthetic was used. The patient developed pneumonia, complicated by pneumococcic meningitis, the diagnosis being established by lumbar puncture. This death was not directly due to the eclampsia, but of course the fatal outcome is to be recorded.

CASE 3.—This was a colored woman, who had marked pulmonary edema on admission. There were no convulsions after the treatment was instituted, and the edema of the lungs was relieved by appropriate treatment. She was delivered by a very easy low forceps operation seventeen hours after admission, as the head, after reaching the perineum, made no further progress. Through a misunderstanding, ether was used as the anesthetic. The pulmonary edema recurred, bronchopneumonia developed, and death resulted. We feel that this fatality was due to the anesthetic. We are, of course, thoroughly cognizant of the fact that general anesthesia, especially when induced by ether, is badly borne by eclamptic patients. We believe that this patient's chances of recovery would have been much enhanced by the employment of spinal analgesia or local perineal infiltration for the delivery.

Thus we have a gross maternal mortality of 10 per cent, or a corrected rate of 3.3 per cent.

As regards the babies, we find that 21 were born alive, and were discharged alive; 9 were stillborn; 24 were known to be alive when the patients were admitted; of these, 21 were born alive, and 3 were stillborn, probably due to the toxemia. Of the 6 other stillborn babies, 2 were known to be dead on admission, 2 others were macerated on delivery and were probably dead on admission (they were also premature), while the remaining 2 (also premature) were probably alive on admission. Thus, of the 9 stillborn babies, 4 were premature, and 5 were at or near term. As will be noted later, there were only 7 operative deliveries; it is possible that resort to forceps in some of the other patients, or earlier employment of operative measures in some of the patients thus assisted, might have slightly lowered the fetal mortality.

We have endeavored to follow a definite routine in the care of these patients, which is altered somewhat to fit the individual case. The treatment may be outlined as follows:

1. On admission, $\frac{1}{4}$ gr. of morphine sulphate is given hypodermically. This has often been given before the patient reached the hospital. It may be repeated in case of slight or moderate restlessness.

2. Five-tenths gram ($7\frac{1}{2}$ gr.) of sodium amytal is given intravenously as soon as it can be prepared, usually within fifteen to thirty minutes. If the convulsions recur, or if there is marked nervous irritability, this may be repeated as often as deemed necessary. Only a few such extra doses were given in this series.

3. As soon as the full effect of the amytal is obtained, the stomach is washed through a Jutte or similar tube, and two ounces of 50 per cent magnesium sulphate are administered through the tube. This drug may be repeated later orally, if indicated.

4. A specimen of blood is secured for chemical analysis.

5. Through the same needle, 300 to 400 c.c. of blood may be allowed to escape, if there is very marked hypertension. This was not done in all our cases.

6. Again using the same needle, 1000 c.c. of a 10 per cent solution of glucose is administered, without insulin. This is usually repeated in twenty-four hours. In most cases, we have given in addition 50 c.c. of 50 per cent glucose by vein twelve to fifteen hours after admission, thinking thereby to ensure better renal function.

7. At a convenient time, a soapsuds enema is given. This is eliminative, and also prepares the rectum for the rectal administration of the sodium amytal, if thought proper. This enema is repeated when needed.

8. Thereafter, sodium amytal, in 3 gr. doses, is given by mouth or by rectum (the more frequent route), every four hours. This is continued until it is felt that all danger of recurrence of the convulsions is past, generally thirty-six to forty-eight hours.

9. Only water or a glucose and water mixture, by mouth or through the Jutte tube, is given until the patient is fully conscious, then a liquid or light diet, rich in carbohydrates, is allowed.

10. If there is edema of the lungs, 1/50 grain of atropine sulphate is administered hypodermically, and repeated in three or four hours, if necessary. We have found that novatropin, 1/20 grain every two hours, is very reliable in such an emergency. Circulatory stimulants are given if indicated.

11. If labor does not supervene spontaneously, induction by one of the approved methods is performed, generally about forty-eight hours after admission. In our series, this was necessary in only eight cases; the catheter was employed 6 times and the bag twice, using sodium amytal intravenously (in doses of 8 to 12 gr.) as the anesthetic.

12. Labor, as a rule, is allowed to terminate spontaneously. Forceps or version may be resorted to in order to shorten the second stage. In this series, low forceps was employed 6 times, and version once. Nitrous oxide oxygen or ethylene may be used as the anesthetic; spinal or local analgesia might be employed to advantage. As noted above, the one patient delivered by low forceps under ether anesthesia died of pulmonary edema and bronchopneumonia. It is possible, as stated in considering the fetal mortality, that more frequent resort to operative delivery might have effected an improvement in this respect; it is also possible that such a policy might have resulted in an increase in the maternal mortality rate.

It will be noted that this treatment consists essentially of sedation by sodium amytal, reinforced by elimination. The intravenous glucose, while highly desirable, might be omitted if conditions were such as to preclude its use. It will be seen that there are five measures resorted to in the treatment outlined above: (1) the preliminary hypodermic administration of morphine sulphate; (2) the exhibition of sodium amytal intravenously, orally, and rectally; (3) elimination by gastric lavage, purgative, and enema; (4) the intravenous use of glucose solutions; and (5) the avoidance of radical operative measures, limiting the procedures to low forceps, breech extraction, version, and the occasional induction of labor.

It might be argued that these adjuvant measures, particularly the use of morphine, are chiefly responsible for the eminently satisfactory results obtained. In answer, we would stress the very prompt suppression of the convulsive seizures following the injection of the first dose of sodium amytal, which is almost dramatic, and the prolonged, quiet sleep which ensues. No such results have been obtained by us in a fairly extensive experience with eclampsia from the use of morphine alone, and while the Stroganoff treatment has proved eminently satisfactory in our hands, the control of the convulsions has been gradually brought about in most cases, rather than being noted as an immediate result, as in this series. The eliminative measures, we feel, are necessary, no matter what form of therapy is employed, and the same we believe to be true as regards the use of glucose.

We feel justified in drawing the following conclusions:

1. That sodium amytal is a safe and efficient hypnotic and sedative, with marked anesthetic properties when given intravenously.
2. That it is of great value in the treatment of eclampsia, as is shown by the fact that, in the 30 cases here reported, the eclamptic convulsions were promptly controlled in every instance. This is in accord with the results obtained by others.
3. That the preparation is worthy of a more extended trial in the treatment of eclampsia, especially as the treatment is simple and may be readily carried out in the home, if hospitalization is not practicable.

SOME PRACTICAL ASPECTS OF HYPOTHYROIDISM

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HAVING become increasingly impressed during the past few years with the importance of hypothyroidism in certain gynecologic and obstetric conditions and having found little emphasis placed upon it in the current literature, it appeared justifiable to present abstracts of a series of case histories in which this condition was the proved causal factor, or in which it was fair to assume that it was predominantly contributory.

Although reference has been made to the lack of emphasis in the literature, it is only right to add that no effort has been made towards an exhaustive review. Occasional case reports have been found in the current literature; Novak has made repeated reference to the condition in his publications; Maranon makes some mention of it in his book "Critical Age"; and other standard works appear to have some cognizance of its existence. The impression gained, however, is that it is a matter of little and only occasional importance.

The present series includes the abstracts of 25 case histories. These are unselected, except that the total number of abstracts has been limited to 25 and has been restricted to what appears sufficient to point the contention that hypothyroidism is neither an infrequent nor an unimportant complicating factor in gynecology and obstetrics. The cases have been divided into an obstetric and a gynecologic group. In the former, there are eight cases, grouped in pairs to emphasize the conditions. In the gynecologic group, there are 17 cases, the last being the only case of hyperthyroidism giving a somewhat similar clinical picture. This case is included to emphasize the possibility of this occurrence and also to emphasize its relative rarity compared to hypothyroidism.

Cases 5, 6, and 7 of the obstetric group were seen in the Gynecological Clinic of the Public Health Center of this city. All others were private patients.

The eight obstetric cases are paired as follows: two of missed abortion, two of habitual abortion, two of pseudocyesis, and two of subinvolution.

CASE 1.—F.W., forty-one years of age. This patient had a miscarriage early in 1923. She had subsequent menorrhagia, with shortening of the interval; tendency to weight gain, and vertical headache. Treatment started November 28, 1923. Metabolism reading: -23 per cent. Complete relief of symptoms.

CASE 2.—F.W., thirty-seven years of age. Miscarriage in 1923. Subsequent menorrhagia and metrorrhagia. Metabolism reading: -19.6 per cent. Treatment started December 19, 1923, with amelioration of symptoms. Subsequently carried to full-term pregnancy and delivered of living child in November, 1924, under thyroid medication.

CASE 3.—F.W., thirty-five years of age. Habitual abortion, miscarriage, or death of fetus. History of empiric, incomplete, antisyphilitic treatment based on marital history. Blood Wassermann negative. About three months pregnant when first seen. Metabolism reading: -10 per cent. Carried successfully through pregnancy on thyroid medication.

CASE 4.—F.W., thirty-eight years of age. Habitual abortion. First seen about sixth week of pregnancy. Metabolism reading: -12 per cent. Carried successfully to term on thyroid medication.

CASE 5.—F.C., twenty-three years of age. Amenorrhea of almost nine months' duration. Carried in Prenatal Clinic until prenatal examination at eight months. Not pregnant. Metabolism reading: -19 per cent. Restoration of menstruation under thyroid medication.

CASE 6.—F.C., twenty-four years of age. Amenorrhea for several months. Carried in Prenatal Clinic until prenatal examination. Not pregnant. Metabolism reading: -13 per cent.

CASE 7.—F.W., twenty-seven years of age. Persistent lochia for three months. Absolute pregnancy gain of eighteen pounds (from 125 to 143 pounds). Metabolism reading: plus 2 per cent. This was the only patient in whom a plus finding was found. Patient was given thyroids gr. i daily. Prompt cessation of lochia. Weight loss of five pounds, with constant pulse between 68 and 75. After first month, weight and pulse remained constant and there was no recurrence of flow.

CASE 8.—F.W., thirty-two years of age. Persistent lochia for two months. Absolute pregnancy gain of thirteen pounds. Metabolism reading: -12 per cent. Cessation of lochia under thyroid therapy.

In the gynecologic group of 17 cases, menorrhagia was predominantly the presenting complaint. This was frequently accompanied by shortening of the intermenstrual interval. In some of the patients, there was lengthening of the intermenstrual interval and, in some, nervousness was the predominating symptom. In all of these patients, a careful search was made for local cause before the taking of a basal rate.

CASE 9.—F.W., thirteen years of age. Very profuse menorrhagia. First seen January 25, 1927. Had already received various types of medication in effort to control flow. Metabolism reading: -15 per cent. Prompt control of very profuse flow under thyroid medication. Gradual establishment of normal cycle.

CASE 10.—F.W., twenty-three years of age. Menorrhagia, for which curettement had been performed three months earlier. Metabolism reading: -10 per cent. Definite improvement in menstrual picture under thyroid medication, during two months under observation.

CASE 11.—F.W., thirty-four years of age. Menorrhagia of gradual onset over past two years. Recently very profuse. Had already had tentative diagnosis of fibroma uteri and confirmatory examination under anesthesia, with probable myomectomy, had been advised. Metabolism reading: -22 per cent. Restoration of normal menstrual cycle under thyroid medication.

CASE 12.—F.W., twenty-four years of age. Irregular and profuse menstruation. Menses appeared at nineteen years of age. Interval three to five months. Flow moderately profuse (eight to nine napkins daily). Metabolism reading: -9 per cent. Later metabolism reading: -19 per cent. Establishment of normal menstrual cycle under thyroid medication. This was one of the earlier patients, coming under observation in October, 1925, and there was considerable hesitation in using adequate doses of thyroid until the later rate of -19 per cent was obtained.

CASE 13.—F.W., forty years of age. Menorrhagia. Metabolism reading: -10 per cent. Complete subsidence of symptoms under thyroid medication.

CASE 14.—F.W., thirty-six years of age. Menorrhagia. Sterility of seven years' standing, following two normal pregnancies. Metabolism reading: -7 per cent. Cessation of menstrual symptoms under thyroid therapy. Conception after ten weeks of therapy.

CASE 15.—F.W., thirty-nine years of age. Menorrhagia. This was one of the earlier patients and the original test gave a slight positive metabolic rate. The rate was repeated after about two years and gave metabolism reading of -13 per cent. Restoration of normal menstrual cycle under thyroid medication.

CASE 16.—F.W., thirty-seven years of age. Menorrhagia and metrorrhagia. Metabolism reading: -14 per cent. Recovery from metrorrhagia and restoration of relatively normal menstrual cycle under thyroid medication.

CASE 17.—F.W., thirty-eight years of age. Irregular menstruation (shortening of interval). History of pelvic plastic and uterine suspension. Subsequent roentgenotherapy, although existence of hypothyroidism had been previously established. Temporary amenorrhea. Recurrence of irregular flow, accompanied by nervousness and "flashes." Metabolism reading: -17 per cent. Disappearance of symptoms under thyroid and amniotin therapy.

CASE 18.—F.W., twenty-six years of age. Profuse menorrhagia. Metabolism reading: -14 per cent. Left observation.

CASE 19.—F.W., twenty-five years of age. Menorrhagia. Previous operation for ovarian cyst with twisted pedicle. Metabolism reading: -7 per cent. Left observation.

CASE 20.—F.W., twenty-eight years of age. Shortening of menstrual flow. Inter-menstrual "spotting." Three-year sterility. Metabolism reading: -15 per cent. Improvement under thyroid medication, but left observation.

CASE 21.—F.W., twenty-four years of age. Menorrhagia. Metabolism reading: -9 per cent. Definite improvement under thyroid medication. As this patient was underweight, it was necessary to watch the thyroid dosage very closely, and it was felt that there was some doubt as to the desirability of adhering to thyroid alone.

CASE 22.—F.W., thirty-six years of age. Dysmenorrhea, slight menorrhagia and extreme premenstrual nervousness. This patient has been under observation only a few months. As the nervous symptoms and dysmenorrhea were predominant, it might be expected that the improvement might be more gradual than with menorrhagia alone. Such has been the case. There has been complete relief from the menorrhagia and improvement in the other symptoms, under thyroid medication. The metabolism reading was -13 per cent.

CASE 23.—F.W., thirty-six years of age. Menorrhagia. Metabolism reading: -2 per cent. Definite improvement under small doses of thyroid. Although this

patient was definitely overweight and gave other physical changes suggestive of hypothyroidism and showed improvement under thyroid therapy, the very slight change in rate rendered the diagnosis questionable.

CASE 24.—F.W., thirty-five years of age. Nervousness and irregular menstruation (lengthened interval). Metabolism reading: -7 per cent. This was considered one of the more doubtful cases. However, there was control of nervous symptoms and restoration of normal menstrual cycle under thyroid medication.

CASE 25.—F.W., twenty-seven years of age. Backache, persistent bitemporal headache, nervousness and shortening of the menstrual interval to three, or even two, weeks. Miscarriage several months before. The backache proved to be orthopedic. The metabolism reading was plus 23 per cent. This case is included to emphasize the possibility of hyperthyroidism, producing very similar symptoms to the much more common hypothyroidism and also because it is the only case of hyperthyroidism found in this series. This latter finding is significant in view of the somewhat hesitant declaration of those who have written on the subject in regard to the relative frequency of the two conditions as a cause of menorrhagia.

TABLE I

DIAGNOSIS	NUMBER	CURED	IMPROVED	UNIMPROVED	LEFT OBSERVATION
Habitual abortion	2	2			
Subinvolution	2	2			
Menorrhagia*	13	8	3		2
Menorrhagia and metrorrhagia	1	1			
Shortening of interval	1	1			
Shortening of flow and intermenstrual "spotting"	1				1
Nervousness and lengthened interval	1	1			
Dysmenorrhea, menorrhagia and premenstrual nervousness	1		1		
Total	22	15	4		3

*The two cases of missed abortion, who presented for treatment for menorrhagia, are included under this heading. Cases treated 19, Cases cured 15 or 79 per cent, Cases improved 4 or 21 per cent.

SUMMARY

The abstracts of 25 case reports are submitted, in 24 of which slight to moderate hypothyroidism existed in company with other symptoms. In 79 per cent of the patients that remained under observation for a sufficient period to justify conclusions, complete relief of symptoms followed thyroid medication. In the remaining 21 per cent, improvement was sufficiently marked to make other treatment unnecessary. In the gynecologic group, menorrhagia was the usual presenting symptom. During the period in which these patients were seen, only one patient was seen in whom the picture of menorrhagia, with shortening of the intermenstrual interval, was accompanied by hyperthyroidism.

CONCLUSIONS

Slight to moderate degrees of hypothyroidism may be very important causal factors in a number of gynecologic and obstetric conditions.

These include amenorrhea and, more frequently, menorrhagia and probably include abortion, miscarriage, premature labor, and death of the fetus.

Hypothyroidism is one of the more frequent causes of menorrhagia and metrorrhagia and should be excluded before resort is had to the curette, radium, x-ray, or abdominal section.

164 MARKET STREET.

SYMMETRICAL CORTICAL NECROSIS OF THE KIDNEYS IN PREGNANCY

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SYMMETRICAL cortical necrosis of the kidneys in pregnancy was first described by Bradford and Laurence¹ in 1898. Jardine and Teacher² in 1910 reported two cases, and Jardine and Kennedy³ in 1913 reported three cases. In 1913 Rolleston,⁴ in a complete review of the literature, was able to collect eleven cases incident to pregnancy. Carson and Rockwood⁵ reported a typical case from this laboratory in 1926. Shriver and Oertel,⁶ reviewing the literature to date (1930), find in all, 37 cases of symmetrical cortical necrosis. They add three cases of their own; one of the patients recovered. Of these 40 reported cases, all but 7 are incident to pregnancy, and of the 33 cases occurring in pregnancy a high percentage have a definite history of retroplacental hemorrhage, there being only one recorded live birth at delivery. To these 40 reported cases we should like to add one which is typical in all respects.

CASE REPORT

Mrs. M. W., aged twenty-six, primipara, was first seen in her home in the late afternoon of May 26, 1931. Her complaint was a dull drowsy feeling and a bilateral backache over both kidney fossae. Some vomiting had attended the drinking of large quantities of water. A moderate vaginal bleeding had been present since morning. Questioning elicited the fact that she had been perfectly well until the morning of the day she was first seen, having worked the day previous. Her last menstrual period occurred in December, 1930 and she had had no vaginal bleeding since. Nocturia had been present twice nightly for the past year, otherwise her history was entirely negative. She had had no prenatal care. A hasty examination revealed a well nourished white female, somewhat restless but rather drowsy. Her face was moderately edematous but no edema was noted on other parts of the body. She stated that her vision was somewhat blurred, and there was a slight acetone odor to her breath. The skin and mucous membranes were very pale. Pulse 96. Temperature 98.2°. Respirations 24 per minute. On abdominal examination no tenderness was elicited over either kidney fossa. A firm, rigid, midline tumor was palpable and was taken to be a pregnant uterus in about the twenty-sixth week of pregnancy. No fetal heart could be heard. A rectal examination confirmed the diagnosis of a pregnant uterus. The external os was contracted and would not admit the tip of the index finger. There was no

vaginal bleeding at the time of examination. The patient was admitted to the University Hospital on the evening of May 26, 1931, quite dyspneic, toxic and exhausted. She could be aroused for short periods of time, but lapsed into a semicomatose condition when undisturbed. The skin was very pale, warm and dry. There was some puffiness around the eyes. The respiratory movements were shallow and rapid, and the patient was apparently having a distinct air-hunger type of breathing. The percussion note was somewhat dull at both bases and a few moist rales were heard over these areas. The heart sounds were clear, regular, but a bit angry. The blood pressure was 180/110.

TABLE I

URINE				BLOOD		BLOOD CHEMISTRY				
HOSP. DAY	VOL. C.C.	SP. GR.	ALBUMIN	R.B.C.	W.B.C.	N.P.N.	URIC ACID	CHLO- RIDES	CO ₂	B.F.
1	25	1.028	2-plus	40 HPF	40 HPF					180/100
2	0	—	—	—	—	55	7.69	295	24	
3	0	—	—	—	—	—	—	—	—	180/100
4	0	—	—	—	—	—	—	—	—	
5	0	—	—	—	—	—	—	—	—	160/40
6	15	—	4-plus	4-plus	4-plus	—	—	—	—	
7	0	—	—	—	—	133	13.3	285	15	140/0

	R.B.C.	W.B.C.	DIFFERENTIAL							
May 28	1,970,000	18,100	Polymorphonuclears 85%— Lymphocytes 11%— Trans. 4%							

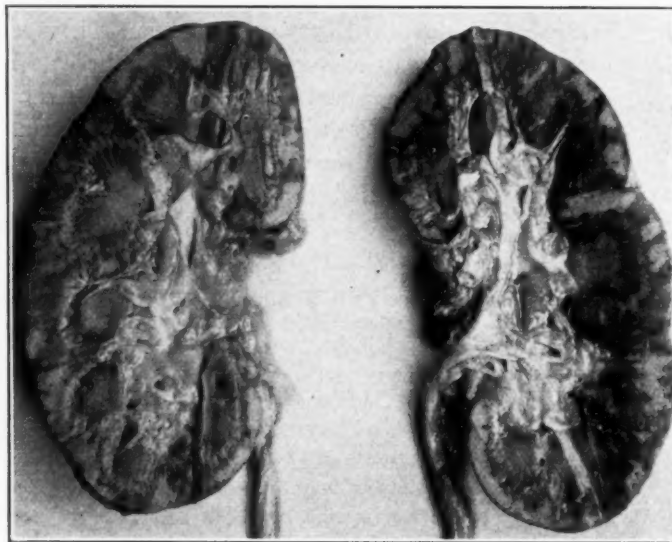


Fig. 1.—Posterior halves of kidneys showing cortical necrosis.

On admission the patient was catheterized and only 25 c.c. of urine was obtained. During the remainder of her hospital stay, only 15 c.c. more were obtained, although she was frequently catheterized in order to obtain a specimen. The patient was quite toxic at all times, being roused with difficulty and falling back into a semicomatose condition quickly. Her systolic pressure varied between 180 and 140. The diastolic pressure was at its highest (110) on admission but rapidly fell until it was practically 0 for the last three days in the hospital.

Glucose was given by vein three or four times daily in the hope of stimulating a diuretic action and to supply fluid and nourishment. Three days after admission, at 8:15 P.M. on May 29, the patient began having rather strong uterine contractions. On examination the cervix was found completely dilated and obliterated with the membranes hanging from the vagina. At 8:35 P.M. a spontaneous delivery of a dead, premature, female child took place. A very large blood clot was expelled and the placenta followed with but little manipulation. The latter was distinctly pathologic in appearance, dark red, mottled with infarcts but seemed to be complete. Following delivery for two days the patient's condition remained approximately the same with no improvement. The same treatment was followed but almost complete urinary suppression persisted, and with a gradually rising nitrogen retention and an increasing acidosis, the patient fell deeper into coma and became more and more dyspneic, and respiration finally ceased on the evening of June 1.

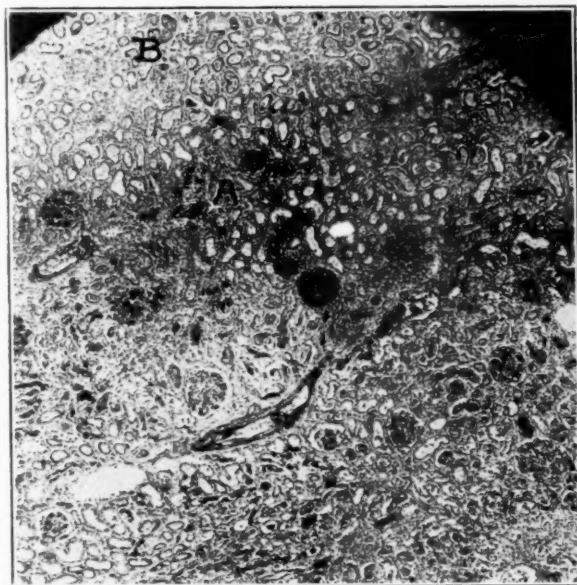


Fig. 2.—Section of kidney cortex. A, Segmental zone of hemorrhage and thrombosis. B, Necrotic tissue.

Autopsy Findings (No. 1709).—This partial necropsy was performed on a well-developed and nourished white female, apparently about twenty-five years of age. The body measured 168 cm. in length and showed the following external evidences of pathology. A generalized subcutaneous edema, most marked about the face and lower extremities; multiple needle puncture wounds in both antecubital fossae with ecchymosis and extravasation of blood; full rounded, firm breasts, from which colostrum could be expressed. A palpable midline tumor mass extended from the symphysis pubis to several cm. below the umbilicus. There was no evidence of external injury, no glandular enlargements and no bony deformities.

An abdominal incision was made from the xyphoid process of the sternum to the symphysis pubis through a moderately obese, edematous abdominal wall. The peritoneal cavity contained 500 c.c. of a clear fluid. The palpable midline tumor was a recently pregnant, subinvolved uterus, which was edematous and boggy and of a deep purplish color. The coils of the small intestines were somewhat distended with gas but were rather equally distributed throughout the upper two-

thirds of abdomen. The liver, spleen, and remaining abdominal viscera were disposed in a normal manner.

The liver and biliary apparatus were removed and examined. The gall bladder contained no stones and the fluid bile could be expressed without difficulty into the duodenum through an unobstructed cystic and common duct. The liver weighed 1,450 gm. and measured 24 by 18 by 8 cm. and externally presented a pale uniform appearance through the capsule. Its consistency was uniformly firm. The cut surface showed a uniform, pale, finely lobulated architecture with no gross areas of hemorrhage or necrosis.

The spleen weighed 180 gm. and measured 13 by 7.5 by 4 cm., and, aside from its firmness and pallor, showed no evident gross pathology either externally or on the cut surface.

The pancreas was heavily infiltrated with fatty tissue, but its size and weight was within normal limits. It presented nothing unusual.



Fig. 3.—Section through necrotic zone showing hyaline thrombus in small arteriole with hemorrhage and necrosis, renal parenchyma.

The adrenals grossly appeared normal.

The kidneys were the site of an interesting condition. These organs were moderately enlarged and embedded in more than the usual amount of perirenal fat. The entire postperitoneal areolar tissue was edematous and water-logged. The right kidney weighed 200 gm., the left 180, and they appeared identical. The capsule stripped off readily, leaving an irregular, finely granular, yellow cortex mottled with hemorrhagic areas and fine red streaks apparently due to capillary dilatation. A few fetal lobulations still existed. On the sectioned surface practically the entire cortex presented a swollen, bulging, pale yellow necrotic appearance, mottled with areas of hemorrhage. This characteristic putty-like appearance extended well down through the columns of Bertini with an accentuated demarcation between the pale necrotic cortex and the pyramids. It appeared almost as an infarction of the cortex. The cortical zone measured 8 mm. on an average in thickness. A few areas of deeply striated functioning cortex remained, irregularly scattered here and there. The right pelvis was somewhat dilated, hold-

ing about 20 c.c., with some mucosal injection. The right ureter was dilated 1 cm. from the brim of the pelvis, proximally. The contracted bladder contained but a few c.c. of a cloudy, turbid, thick urine. The edematous, boggy uterus when opened showed a posterior fundal placental site with a few placental fragments

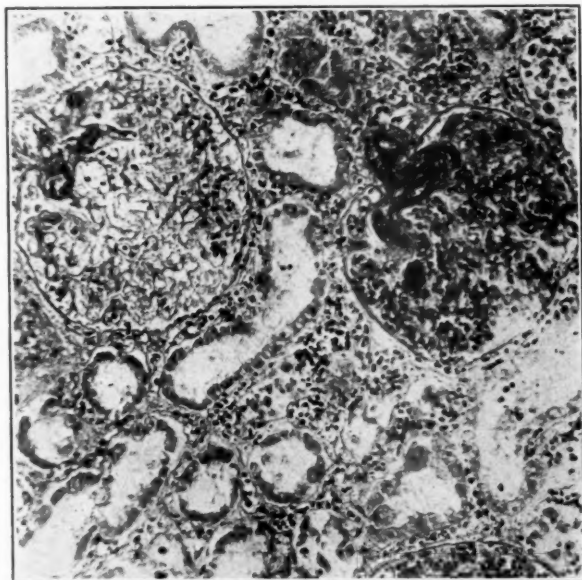


Fig. 4.—Section through necrotic zone showing thrombi in capillaries of glomerular tufts.

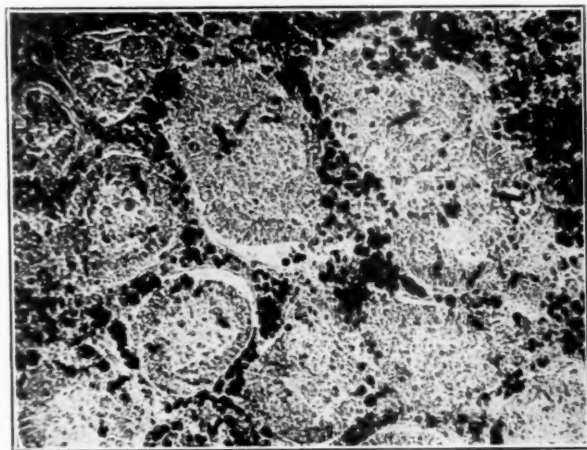


Fig. 5.—Section through the necrotic zone, stained by Herxheimer's method for fat, shows globules of fat in the intertubular capillaries. There are also small droplets of fat in the necrotic tubular epithelium.

and fetal membranes remaining. The thinned out cervix showed some laceration and admitted three fingers. The remaining pelvic adnexa appeared normal for this stage in pregnancy. The gastrointestinal tract showed nothing unusual. Autopsy was limited to abdomen.

MICROSCOPIC

Numerous sections from both kidneys were studied. In the H. & E. stained sections there was some fibrous thickening of the capsule and some detachment from the cortex in areas, apparently due to edema. Large topographic sections gave an appearance of patchy infarction, large areas of the cortical element, both tubules and glomeruli, being in a state of coagulation necrosis. In spite of this apparent necrosis, the general architectural arrangement was preserved without dissolution. The nuclear elements of cells in these zones were fragmented, pyknotic, or entirely absent, the pale pink staining cell wall and cytoplasm remaining as a shadow. A fairly sharp line of demarcation was present between these necrotic zones and the surrounding, functioning cortex. Along this margin there was extensive leucocytic infiltration and extravasation of red blood cells into and between tubules and into glomeruli. A narrow rim of fairly well preserved cortical tissue was present just under the capsule, showing that this area had a capsular blood supply which was not involved in this process. The majority of arterioles in the zone of coagulation necrosis showed intimal roughening and hyaline thrombosis. Frozen sections stained by Herxheimer's method were interesting because of the unusual amount of intravascular fat. The thrombosed cortical vessels and intertubular capillaries, as well as glomerular tufts were practically loaded with globules of fat. The fat present was not entirely confined to the vascular system, however, for many fine droplets were observed in the degenerated tubular epithelium.

DISCUSSION

In reviewing the literature on this subject, a relatively clear-cut clinical entity was found. Several instances of cortical necrosis have been reported during the course of infectious diseases in both sexes, even in children (diphtheria "Stoeckenius," pneumonia and peritonitis "Herzog"¹⁸), but by far the majority of these 40 cases have occurred in females, from the fourth month to term, following some accident during pregnancy, usually retroplacental hemorrhage. In only one instance has the fetus been born alive (Jardine and Kennedy). In this case twins were delivered. There may be no antecedent history or clinical signs suggesting renal involvement beforehand, but edema is common to a greater or lesser degree preceding the urinary suppression (anuria). Anuria is one of the most constant symptoms and is usually complete or practically complete, coming on from several days before delivery to several days postpartum and continuing until death. Vomiting, although a rather persistent and outstanding symptom in this case, is not the rule. A gradually increasing nitrogen retention with a rather rapid accumulation of creatinine, as opposed to its slow rise in such conditions as chronic interstitial nephritis, is an outstanding feature, as pointed out by Shriver and Oertel.

As regard blood pressure, only a few cases are available, where repeated determinations have been made. In these there is a tendency for the pressure to drop with the progress of the disease, but whether this fall has a cause or effect relationship to the renal condition cannot be determined.

The distribution of this aptly named symmetrical cortical necrosis clearly indicates that the pathologic changes are on a circulatory basis, but whether the vascular lesion be thrombotic, embolic or a vasoparesis with stasis as suggested by Shriver and Oertel, is not as yet definitely proved. There is no doubt but that there are thrombi in the majority of arterioles in the necrotic cortex of this kidney. This thrombosis is only present in the segmentary level of cortical necrosis. The topography of the lesion alone speaks against an embolic phenomenon, for it would be unusual for multiple emboli to choose in such a regular manner this particular level in the kidney cortex. Fat embolism apparently bears no causal relationship to this condition. Wright¹¹ in an article to be published on this subject finds areas of advanced tubular necrosis in a fatal case of fat embolism. The necrosis in his case, however, is not generalized and is without regular or symmetrical distribution. The absence of discernible intravascular fat in other organs rules out a generalized fat embolism. It is a well known fact that during the latter half of pregnancy there is a hyperlipemia. Slemmon and Stander⁹ found a gradual increase in the fat content during the latter half of pregnancy, there being 900 mg. per 100 c.c. of maternal blood at term. The cause of this hyperlipemia was unknown but was thought to be probably due to a general change in lipoid metabolism in preparation for lactation. There was no departure from this gradual increase in the toxemias. The cholesterol and lecithin content of the blood are also gradually increased during the latter half of pregnancy. Tyler and Underhill¹⁰ found an increase in the fat content as early as the third month. From a study of this case it is evident that some local circulatory disturbance has unmasked this intravascular fat in the kidney, and we feel that it is the result rather than the causal factor in this necrosis. If a vasoparesis with stasis be the etiologic factor for this necrosis, some vascular irritant must be searched for which has a special affinity for renal cortical vessels.

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DELAYED CHLOROFORM POISONING

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IN 1924 we reported a chemical study of a case of delayed chloroform poisoning,¹ in which the outstanding features were an increased destruction of protein, a lowering of the alkali reserve of the body, a disturbance of liver function, and a moderate degree of renal insufficiency. Since that time, we have studied experimentally the immediate effect of chloroform on the liver tissue as well as on the blood and urine constituents,² when we found that in the dog it produced pronounced central necrosis of the liver lobule and less marked kidney changes as soon as twenty minutes after its administration. Immediately following the administration of chloroform, the blood analyses revealed a hyperglycemia, whereas in delayed chloroform poisoning hypoglycemia is the usual finding. In our 1926 article,² we discussed the various factors that may play a rôle in the production of the hyperglycemia and the other abnormal chemical findings immediately following chloroform anesthesia; consequently this paper is concerned only with delayed chloroform poisoning and is based upon a fatal case recently occurring on our service.

The clinical history of our patient is as follows: Unit History No. 36,217. A twenty-seven-year-old colored primigravida, who had her last menstrual period June 15, 1930, was admitted March 22, 1931, with a history of beginning labor. The family and personal history was negative, as likewise the Wassermann. Examination showed a well nourished individual. Heart and lungs normal. Blood pressure 120/75; urine negative for albumin. A normal sized child lay in L.O.T., head engaged. Fetal heart in left lower quadrant, rate 120. Cervix just admitted finger tip. Occasional labor pains.

Labor progressed very slowly, with infrequent and weak pains. Castor oil and quinine were given on the morning of March 23, 1931. At 6:00 P. M., March 23, 1931, the cervix was 3 cm. dilated and became fully dilated at 7:30 P. M. the following day. On account of poor cooperation the head was delivered by Ritgen maneuver at 8:18 P. M., March 24, 1931, when a second degree tear was sustained. The child was slightly asphyxiated but cried within a few minutes, weighed 3170 gm., and presented a biparietal of 10 cm. The placenta separated spontaneously and was expressed at 8:28 P. M., March 24, 1931, by Duncan method. Placenta and membranes intact. Blood loss 100 c.c. Both patients returned to ward in good condition.

Whiffs of chloroform were administered during the second stage, but full anesthesia was employed for one-half hour during the repair of the perineal tear. Chloroform was used instead of gas oxygen, owing to the fact that the regular delivery room anesthetist was not available at the time, and the amount used measured 2½ ounces.

On the third day after labor, the patient became increasingly drowsy and failed to rally, dying in a convulsion on the next day.

A single catheterized specimen at 10:15 A. M., March 28, 1931: volume 75 c.c.,

total nitrogen 0.487 gm., urea nitrogen 0.147 gm.—30.2 per cent of total nitrogen, ammonia nitrogen 0.121 gm.—24.8 per cent of total nitrogen.

At noon, March 28, 1931: volume 250 c.c., total nitrogen 0.515 gm., urea nitrogen 0.161 gm.—31 per cent of total nitrogen, ammonia nitrogen 0.180 gm.—34.9 per cent of total nitrogen.

Blood taken at 5:30 P. M., March 27, 1931, showed nonprotein nitrogen 88.2 mg. per 100 c.c. blood, uric acid 11.7, sugar 88, CO_2 combining power 24.2 volumes per cent, chlorides 435 mg. per 100 c.c. blood.

Blood taken at 11:00 A. M., March 28, 1931, nonprotein nitrogen 134.1 mg. per 100 c.c. blood, urea nitrogen 66.7, uric acid 12.6, sugar 182, CO_2 combining power 17.8 volumes per cent, chlorides 415 mg. per 100 c.c. blood, creatinine 4.6, amino acids 15.5, O_2 content (venous) 14.1 volumes per cent, O_2 capacity 17.5.

Comparing these findings with those we reported in 1924, it is found that both patients showed an increased excretion of nitrogen in the urine, with a marked increase in ammonia nitrogen and a decreased urea nitrogen. The two patients also presented almost identical blood constituent

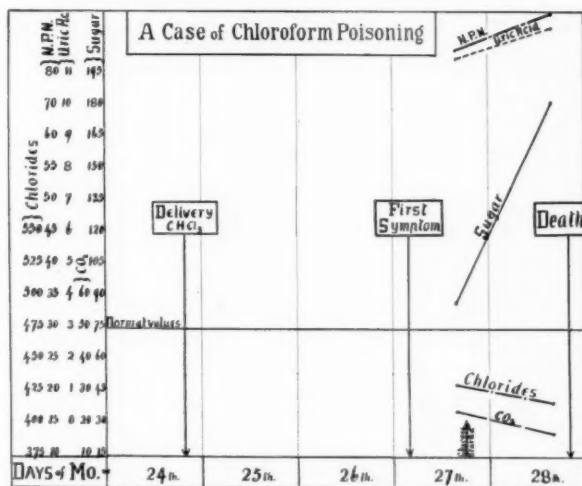


Fig. 1.

concentrations. The figures in the present case are so striking that we have plotted a few of them in Fig. 1.

Autopsy revealed typical central necrosis of the liver; the kidneys were normal; and so were all the other organs. Including the present one, five cases of delayed chloroform poisoning have occurred in this service since 1894. In two of them we have had an opportunity to carry out fairly complete chemical studies on the urine and blood. From the evidence thus far available, we may state that the outstanding characteristics of delayed chloroform poisoning are as follows:

1. As little as two ounces of chloroform, administered to induce surgical anesthesia, is sufficient to produce delayed poisoning.
2. The first symptom or indication of delayed poisoning usually appears two to three days following the use of the drug.
3. Vomiting or jaundice may or may not be present.
4. Drowsiness, stupor and coma always develop.

5. Autopsy findings always reveal central necrosis of the liver.
6. Kidney function may or may not be greatly impaired.
7. Urinalysis always shows increased nitrogen excretion, with high ammonia coefficient and low urea nitrogen.
8. Blood studies show an increasing nitrogen retention, low chloride concentration, marked uric acid increase, decreased alkali reserve to a level of true acidosis, a high concentration of amino acids, and a sugar level at or slightly below normal.
9. The mortality of this condition was 80 per cent in our five cases.

COMMENT

We have previously¹ discussed the theory relating to the "fixing" of chloroform by all or certain of the lipoids. Marked susceptibility to liver injury from chloroform has been noted in animals on a diet rich in fats.² Following their brain-feeding experiments, Davis and Whipple⁴ believe that their results in starvation disprove Opie's theory of chloroform "fixing" by fats.

Liver injury accompanied by a suddenly developing acidosis appears to be the most striking characteristic of delayed chloroform poisoning. The treatment in our last two cases, both of whom died, appears to be open to criticism in that the acidosis was not adequately treated. In the present case, we administered sodium bicarbonate by rectum, but the alkali was not retained. Active intravenous alkali therapy should have been instituted immediately after it became known that the CO_2 combining power had dropped to below 20 volumes per cent. The liver injury is best treated by the continuous intravenous administration of glucose. This was done in the present case, and its effect is shown by the blood sugar rising from 88 to 182 mg. per 100 c.c. blood. In general, it may be said that after delayed chloroform poisoning has developed our only hope lies in glucose therapy and antiacidosis measures.

We are reporting this case, however, particularly for the purpose of stressing the danger of using chloroform in any surgical procedure. Whiffs of it, with an abundant supply of air, may be permissible when the child's head is passing over the perineum, provided no other anesthetic is available. On the other hand, the use of chloroform during perineal repair seems absolutely contraindicated, as here deep anesthesia is necessary. We realize that chloroform is sometimes used in surgical procedures, but great experience and good anesthesia technic are essential. As most of us are not schooled in the proper administration of this agent, it would be better never to use it in any surgical procedure, however simple. Finally, we feel that many deaths occurring two to four days following the use of chloroform, are really due to delayed poisoning, but the relation is not recognized so that death is attributed to some other cause.

CONCLUSIONS

1. The mortality in delayed chloroform poisoning is about 80 per cent.
2. Intravenous glucose therapy and antacidosis measures, such as sodium bicarbonate intravenously, offer the only hope of recovery.
3. Chloroform should not be used in any surgical procedure, except by an expert anesthetist especially schooled in its use.
4. The only place for chloroform in obstetrics is late in the second stage, when it should be administered in whiffs (anesthesia a la reine); and even then it should only be used when no other anesthetic is available or indicated.

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LEUCOPLAKIA OF THE UTERINE CERVIX

OTTO S. KRETSCHMER, A.M., M.D., DENVER, COLO.

LEUCOPLAKIA of the cervix is a rare condition, only ten cases being reported in the literature up to 1927. It manifests itself with no typical symptomatology and occurs mostly after the third decade of life. The etiology is unknown, though various forms of mechanical, bacteriologic and chemical irritations probably are involved.

As elsewhere, leucoplakia of the cervix must be considered precancerous and the length of time required for a cervical leucoplakia to develop malignant changes ranges from two years (von Franqué) to eight years (Verdalle¹).

The characteristic histopathology of cervical leucoplakia is brought out in the illustrations. When malignant changes occur within a leucoplakia, these are similar to those observed in like growths on mucous surfaces elsewhere. However, when stratified squamous epithelium is desquamated in the formation of an erosion on the cervix, during the stage of healing, the regenerating epithelium may grown down into the lumina of the glands so denuded, without thereby developing a malignant character (Fig. 5).

In diagnosing cervical leucoplakia, reliance must be placed, not upon the symptomatology, which is slight, but upon cervical inspection in all cases presenting pelvic symptoms of any kind. Smaller lesions are best seen with an instrument devised by Hinselmann called the colposcope. Following West's² suggestion for detecting cervical cancers, it is well to conduct periodic pelvic examinations of women of middle age in order to discover cervical leucoplakias. If the lesion be small, complete excision as recommended by Bloodgood³ for skin tumors, is the method of choice and pathologic examination of the tissue is car-

ried out at leisure. Following excision, radium is applied according to the technic described below. For larger lesions, again following Bloodgood's recommendations, excision of a piece of tissue with the cautery knife and immediate examination of a frozen section should be performed. Hinselmann and Esser⁴ have found that apparently complete removal of a leucoplakic spot may be followed by recurrence. No recurrence is likely if radium is properly applied.

In the treatment of cervical leucoplakia, cauterant chemicals have been found ineffectual. Amputation of the cervix is carried out routinely by Hinselmann⁵ according to the method of Bonney. As in one of my cases, the leucoplakia may extend through the cervical canal into the uterine cavity. When such is the case, amputation is inadequate. Moreover, whenever radium is available, in the absence within the leucoplakia of malignant changes, surgery is not necessary. Radium will, according to Sanford Withers, eliminate nonmalignant leucoplakia readily when properly applied.

The latter's technic, as given to me, is as follows:

Radium in sufficient quantity to cause destruction of the cervical mucous membrane is applied against the entire cervix. For this purpose the radium is enclosed within a 2 mm. thick lead cup or saucer and placed against the cervix. By this method 25 to 50 mg. hours per square centimeter of surface involved are applied. When the leucoplakia extends into the cervical canal or even into the uterus, a capsule of radium may be inserted into the former up to the internal os, and a dose of 250 to 400 mg. hours, with as little filter as possible is given. One application of radium is all that is usually necessary to clear up the leucoplakia.

When precancerous or early carcinomatous changes are present within the leucoplakia, radium is still the treatment of choice.

CASE REPORTS

The following cases were referred to me by Sanford Withers.

CASE 1.—Mrs. S. B., widow, aged sixty-nine. Until the present illness she had always been well. She had given birth to 6 children. Had always had normal menses until her menopause at fifty-two years of age.

Present complaint: For nine weeks she had flowed a moderate quantity of bright red blood.

Pelvic examination showed the cervix and almost the entire uterus protruding from the vaginal orifice. A collar of lusterless white mucous membrane covered the cervix, with an erosion of dark red color 6 mm. in diameter passing from the cervical canal outward. Tubes and ovaries seemed normal to palpation. Blood Wassermann was negative.

Vaginal hysterectomy was performed and sections were made from specimen removed (Figs. 1 to 5).

Pathologic examination disclosed a leucoplakia of the uterine cervix, no malignancy present. Erosion of the cervix. Patient has shown no malignant metastases after seven months.

CASE 2.—Mrs. S. S., housewife, aged forty-one. Had always been well. One child. No miscarriages. Menses regular but painful.

Present complaint: had leucorrhea and spotting of blood.

Examination showed a uterus and a cervix freely movable. The body of the uterus had a feeling of increased density. The cervix was enlarged and eroded at

two points, one of which was surrounded by an area white in color. There was a small nabothian cyst. Blood Wassermann negative.

Excision was performed on the entire leucoplakic area 6 by 4 mm. in size and paraffin sections made (Fig. 6). Following this radium was applied.

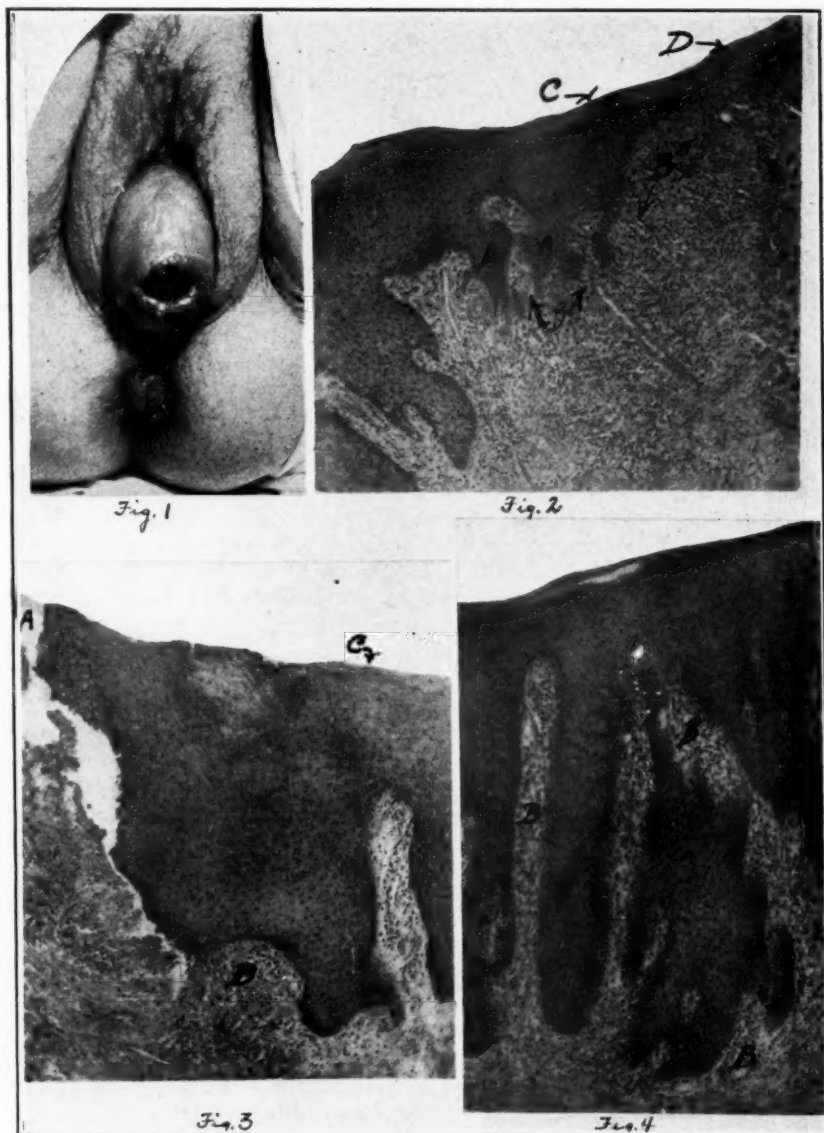


Fig. 1.—Prolapsed cervix and uterus, showing dark area of erosion and whitish collar of leucoplakia in the cervix. (Case 1.)

Fig. 2.—Leucoplakic area showing diffuse round cell infiltration (B) at the margin and beneath irregular rete Malpighii pegs (A). Latter are bizarre and atypical. Cornification present (C). Sudden transition to more normal epithelium at (D). (Case 1.)

Fig. 3.—A break in the epithelium due to ulceration (A); round cell infiltration beneath and between rete pegs (B). Stratified squamous epithelium greatly thickened, cornified epithelium covering the surface (C). (Case 1.)

Fig. 4.—Irregular and bizarre rete pegs which are atypical, having precancerous appearance. Round cell infiltration between and within rete pegs. (Case 1.)

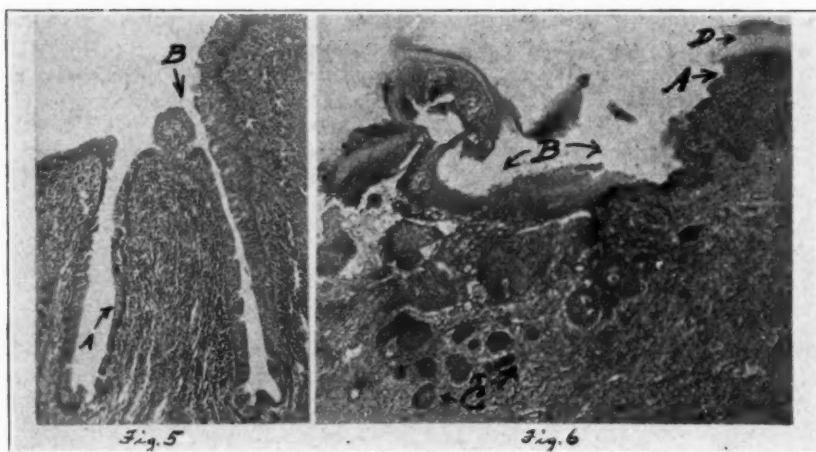


Fig. 5.—Downgrowth of stratified squamous epithelium of leucoplakia into a gland at (B). Contrast this with the single layer of columnar epithelium at (A), in a similar gland. Atypical but not malignant. (Case 1.)

Fig. 6.—Leucoplakia showing thickened stratified epithelium (A); ulcerous excavation (B); diffuse round cell infiltration beneath epithelium. A number of detached epithelial cell nests (C) which constitute a very early change in a malignant direction underneath the leucoplakic epithelium. Cornification present (D). (Case 2.)

Examination showed a leucoplakia with early squamous cell carcinoma.

No recurrence of either process after eight months.

CASE 3.—Mrs. K. C., widow, sixty-five years of age.

Past History: Widow for eighteen years; married for fifteen years previously. Had two children, one well, the other with heart disease. Had been well all her life. Menses commenced at eleven years; always regular; no dysmenorrhea; duration three days; scant flow; menopause at forty years of age. No difficulty at that time. No operations at any time.

Present complaint: Bloody vaginal discharge for one month.

Onset and course: For one year patient has had urinary frequency at night, 7 or 8 voidings each night. Complained then of a thin whitish discharge from the vagina. Three months ago this became profuse, yellow and odorous. Two months ago there occurred a bloody discharge without clots. Since then she has been spotting blood.

Examination revealed a well-nourished woman; lungs, heart and abdomen were negative. Vaginal examination showed a second degree prolapse of the uterus, and the anterior lip of the cervix enlarged to about $2\frac{1}{2}$ by $1\frac{1}{2}$ inches and consisted of a cauliflower-like growth of tissue which bled easily when manipulated and was of whitish coloration. There was present bleeding from the cervical canal. The uterus and cervix were freely movable and the adnexa were not palpable.

Microscopic examination of the tissue of the cervix after hysterectomy showed a definite thickening of the stratified squamous epithelium of a leucoplakic character as in Case 1, and no premalignant changes were evident.

Pathologic diagnosis: Leucoplakia of the uterine cervix. No malignancy.

Patient well after eight months.

SUMMARY AND CONCLUSIONS

1. Large leucoplakias of the cervix are considered rare.
2. Simple leucoplakia is a benign condition, but cancer may eventually become engrafted upon it in a considerable number of cases. Hence it is well to treat it as a precancerous condition.

3. Leucoplakia of the cervix displays few symptoms, none of which are pathognomonic, direct examination of this organ alone leading to its detection. Consequently, periodic and routine examinations of women after thirty years of age are recommended.

4. Pathologic examination of leucoplakic tissue removed with proper technic in cases of cervical leucoplakia is urged to detect malignant changes.

5. The most effective and rapid treatment of nonmalignant leucoplakia of the cervix is the application of radium.

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REPUBLIC BUILDING.

THE MODIFICATION OF THE ASCHHEIM-ZONDEK TEST BY THE USE OF BLOOD SERUM. PRELIMINARY REPORT*

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WHILE the technic of the Aschheim-Zondek test is comparatively simple, there are two practical disadvantages, including the multiple injections of the mice extending over a period of three days, with subsequent examination at the end of one hundred hours, and likewise the toxicity of the urine with death of the mice in a high percentage of cases, even when the urine is detoxified with ether or sulphosalicylic acid.

In an attempt to overcome these disadvantages, a series of experiments were performed, using blood serum instead of urine for the mouse inoculation. Parallel tests on the urine of the same cases, using the Aschheim-Zondek technic were performed at the same time.

Technic.—Blood was collected from the vein in the usual manner. After coagulation, it was centrifuged and 1 c.c. of blood serum injected subcutaneously into each of two or three immature female mice, weighing 6 to 8 gm. The animals were killed after seventy-two hours and examined according to Finkel's method for hyperemia and enlargement of the uterus.

In the first series of cases the tests were made with serum from women six to eight months pregnant, specimens of blood and urine being obtained from patients in the Prenatal Clinic of the Bridgeport Hospital through the courtesy of Dr. H. E. Waterhouse.

*Submitted for publication, October 19, 1931.

TABLE I

NO. CASES	AMT. OF SERUM	MICE			CONTROL	ASCHHEIM- ZONDEK URINE TEST	REMARKS
		A	B	C			
(1) 6 mo. gravid	1 c.e.	+	+	+	-	+	Large area of de- haired scar on abdomen of mice
(2) 6 mo. gravid	1 c.e.	+	-	+	-	+	Small B mouse be- low four grams
(3) 8 mo. gravid	1 c.e.	+	+	+	-	+	
(4) 8 mo. gravid	1 c.e.	+	+	+	-	+	Scab on abdomen
(5) 7 mo. gravid	1 c.e.	+	+	+	-	+	Scab on abdomen
(6) 7 mo. gravid	1 c.e.	+	+	+	-	+	
(7) 7 mo. gravid	1 c.e.	+	+	+	-	+	Scab on abdomen
(8) 7 mo. gravid	1 c.e.	+	+	+	-	+	

The mouse reaction after a single injection of serum was similar in all respects to that obtained from the urine of the same cases. The only exception was in Case 2, where one of the three mice was very small.

Similar results were obtained in ten cases of early pregnancy, ranging between five days to four months.

All 10 cases (Table II) showed a positive reaction with the serum; and in 7 cases on which it was done, the Aschheim-Zondek test on the urine was also positive.

In the above series serum and urine from sexually mature, healthy, young nonpregnant women were used. In these cases the specimens were taken between the end of the menstruation up to seven days before menstruation. Specimens were not collected later in the menstrual cycle in order to avoid any possible premenstrual reaction.

In all cases the tests, with both the urine and the serum were negative.

SUMMARY

1. A modification of the Aschheim-Zondek test for pregnancy is presented in which a single subcutaneous injection of 1 c.e. of blood serum into an undeveloped female mouse of 6 to 8 gm. is used.

2. A reaction, in all respects similar to the Aschheim-Zondek is obtained after an interval of seventy-two hours.

3. With the above method, there has been little mouse mortality.

4. It seems reasonable to assume that in pregnancy there is an increased amount of female sex hormone in the blood serum and that

TABLE II

NO. CASES	AMT. OF SERUM	MICE		CONTROL	ASCHHEIM-ZONDEK URINE TEST	REMARKS
		A	B			
(1) 12 wk. amenorrhea Mrs. B.	1 c.e.	+	+	-	Not done	
(2) 8 wk. amenorrhea Mrs. McC.	1 c.e.	+	+	-	Not done	Scab on abdomen of both mice
(3) 5 days amenorrhea Mrs. M.	1 c.e.	+	+	-	Positive	Scab on both mice
(4) 13 wk. amenorrhea Mrs. L.	1 c.e.	+	+	-	Not done	
(5) 12 wk. amenorrhea Mrs. M.	1 c.e.	+	+	-	Positive	
(6) 8 wk. amenorrhea Mrs. S.	1 c.e.	+	+	-	Positive	
(7) 3 wk. amenorrhea Mrs. L.	1 c.e.	+	+	-	Positive	
(8) 10 days amenorrhea Mrs. C.	1 c.e.	+	+	-	Positive	
(9) 8 wk. amenorrhea Mrs. R.	1 c.e.	+	+	-	Positive	
(10) 6 wk. amenorrhea Mrs. H.	1 c.e.	+	+	-	Positive	

TABLE III

NO. CASES	AMT. OF SERUM	MICE		CONTROL	ASCHHEIM-ZONDEK URINE TEST	REMARKS
		A	B			
(1) Miss McA.	1 c.e.	-	-	-	Negative	13 days, post menses
(2) Miss L. P.	1 c.e.	-	-	-	Negative	10 days, post menses
(3) Miss M. T.	1 c.e.	-	-	-	Negative	14 days, post menses
(4) Miss P. L.	1 c.e.	-	-	-	Negative	20 days, post menses
(5) Miss McM.	1 c.e.	-	-	-	Negative	20 days, post menses
(6) Miss C. L.	1 c.e.	-	-	-	Negative	10 days post menses

its increase in the urine is due to this fact rather than to any selective action of the kidney.

I wish to extend my earnest thanks to Dr. H. LeBaron Peters for the sincere cooperation I received in his Laboratory at the Bridgeport Hospital.

NOTE: Since this article was submitted for publication, tests have been carried out in seventy pregnant women at the Methodist Episcopal Hospital, ranging from the second to the eighth month. The reaction was positive in every case, with the loss of only six mice in a series of 140 used for the tests.

ATRESIA ANI VAGINALIS

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ATRESIA ani vaginalis or vaginal anus is a term broadly applied to a developmental defect in which the anus is absent from its usual location and the rectum terminates in the posterior wall of the vagina somewhere between the fornix and the fourchette. Vulval anus, vestibular anus, atresia ani hymenalis are synonymous terms limiting the rectal opening to a definite location.

Anorectal defects result from faulty embryologic development and the classification of these malformations varies but in all cases depends on the pathologic anatomy of the structures involved. Vaginal anus is segregated in that group of conditions in which the rectum terminates abnormally in some portion of the genitourinary tract. Brenner¹ states that this group of malformations makes up 40 per cent of all cases. As the rectum and genitourinary tract open into a common cloaca early in embryologic life, an arrest of the development of the tissues between the rectal and genitourinary portion of the cloaca will result in the rectum opening in some portion of that tract.

No reliable statistics are available of the incidence of anorectal defects in general or vaginal anus in particular, but scores of individual cases and a few fairly large series of cases of vaginal anus have been reported. These reports are in the majority of cases of infants and children, and as the mortality is high, relatively few occurrences are reported in adults. Thirty-five of a series of 51 cases reported by Buckmaster² occurred in children under ten years of age. In 15 cases of this type reported by Brenner, 14 were under ten years of age.

The occurrence of cases of vaginal anus in infants and children is of slight importance to the obstetrician, but pregnancy occurring in an individual afflicted with such a malformation may be the basis for the development of serious complications. Fecal contamination of the parturient canal is unavoidable and the patient suffers all the risks of developing a postpartum infection, as well as the late consequences of lacerations with loss of sphincter control.

Following the delivery of the patient whose case is here reported, a study of the similar cases recorded in the literature was undertaken with the view of determining the results obtained in their management. Only eight cases were found, which with the present one makes

a total of nine reported to date. It is possible that some have been overlooked as was true in the 53 cases of vaginal anus collected by Buckmaster,² who stated that they "comprised most of those on record." Dwight³ however in 1895, the following year, reported a new case and mentioned several others, none of which were recorded by Buckmaster.

Following is an abstract of the eight previously reported cases of vaginal anus, the first three being included in Buckmaster's report and the fourth in Dwight's.

CASE 1.—(M. Fournier¹) Woman in labor five days. Rectum had to be emptied through large opening in vagina before labor could be terminated. Results not given.

CASE 2.—(Cook²) Deformity discovered while patient was in labor. Results not given.

CASE 3.—Patient had three children. Malformation accidentally discovered during examination for suspected disease of the rectum. Neither she, her husband, nor the accoucheur had suspected any abnormality. The anus was imperforate.

CASE 4.—(Tuck) Mentioned by Dwight.³ Discovered during labor, rectum opening into vulva below the hymen. Spontaneous labor. Good sphincter control resulted.

CASE 5.—(Le Masson⁴) Rectal malformation discovered during labor. The rectum terminated in the fossa navicularis, separated from the vagina by thin membrane. Spontaneous labor with slight lacerations on either side of the anovaginal septum but no laceration through this membrane. Repair produced good results and patient and baby were discharged on the twentieth day postpartum.

CASE 6.—(Smiley⁵) Discovered during labor. The rectum opened in posterior vaginal wall two inches above vaginal orifice. Prolonged labor terminated by forceps, and laceration of tight perineum. A moderate postpartum infection developed which subsided by the thirteenth day. Result continued sphincter control.

CASE 7.—(Pascal⁶) Discovered during labor. Rectum opened in posterior wall of vagina 2½ inches from the introitus. Sphincter muscle well developed. Contracted pelvis, cesarean section chosen as method of delivery, being the first one recorded. Result stated as unsuccessful.

CASE 8.—(Hipsley⁷) The rectal malformation in this instance was used as an indication for performance of cesarean section with the object of preventing loss of sphincter control. Results good.

Following is a more detailed report of the case which occurred in the White Memorial Clinic.

CASE REPORT

Mrs. E. B. M. entered the hospital September 9, 1928, in active labor, pains having started two hours before admission. She was nineteen years old, a primigravida, and one week before estimated term. The fetus was in right occipito-posterior. The anus was found to be absent from its usual location and the rectum terminated in the posterior portion of the vagina at the fourchet. Only a thin mucous membrane separated the vaginal and rectal passages. No evidence of sphincter ani muscle found, but the patient had normal control over the bowel movements except after the use of cathartics.

Course of Labor: The second stage of labor was allowed to progress until rupture of the anovaginal septum was imminent. Performance of a lateral episiotomy on each side carrying the incision lateral to the rectal opening, allowed the head to descend and push the rectum toward the sacrum, the delivery being terminated

spontaneously. The child weighed 7 pounds 8 ounces (3420 gm.). Since the episiotomy incisions were not extended by laceration, the previous anatomic relationship was reestablished by the repair. The puerperium was attended with no morbidity and the sphincter action remained satisfactory.

The mother of the patient stated that the patient was unable to have any bowel movements following birth. The attending physician performed an operation for this condition after which the development of the child was uneventful.

I communicated with the physician, and he stated that an incision was made through an imperforate anus and the opening dilated systematically until normal bowel movements occurred.

The unusual termination of the rectum was not noted by the physician and evidently no attempt was made to establish the anus at the normal location. I have been unable to find a single instance of the occurrence of pregnancy in an individual who had been operated upon for an imperforate vaginal anus.

Operations of various types have been described for correction of such rectal defects with the object of establishing the anus at the usual location. Though these efforts are imperative in some instances to save life, yet in any case where the rectum terminates in the vagina and with normal control present, avoidance of operative procedures is suggested by the results of the cases above reported, as in no case was loss of sphincter control definitely stated and unsatisfactory results were stated only once in the case with contracted pelvis. Pregnancy occurring with such an anomaly presents perhaps the greatest chance the patient would undergo of developing complications, and the absence of such in the reported cases is significant.

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1913 MARENGO STREET

REPORT OF A CASE OF LITHOPEDION CARRIED FOR FORTY YEARS

BY LAWRENCE S. OTELL, M. D., WASHINGTON, D. C.

PATIENT E. V., aged seventy-five, white female, entered the hospital complaining of weakness and paralysis.

She had always been unusually well and had no serious illnesses or operations. Married for forty-five years. No children. Forty years ago thought that she was pregnant and had usual signs and symptoms. After several months she noticed a lump in her left side which gradually, over a period of months, appeared to move to the midline and finally disappear entirely. Menstruation reappeared and there was no alteration up to the time of the menopause, which was without undue incident.

The present illness began three or four years ago with generalized muscular weakness and inability to use legs. Gradual loss of vision in left eye and dimness of vision in right. There was no definite paralysis or loss of sphincter control, though there was some urgency.

On admission blood pressure was 250/120. Somewhat obese elderly white woman, weak but not acutely ill. Left pupil did not react to light or produce consensual reflex. Right reacts and produces consensual reflex. Left disc shows complete diffuse grayish pallor with only two small vessels emerging from center. Right shows diffuse grayish pallor, not as marked as on left, however. Septum deviated to right. Dental caries; pyorrhea and gingivitis. Bilateral facial weakness more marked on left. Heart slightly enlarged to left. Sounds totally irregular with numerous extrasystoles. Left systolic murmur over precordium, not transmitted. Peripheral vessels sclerotic. Abdomen extremely hard, nodular mass in midline just above pelvic brim, apparently within or connected with uterus, as disclosed by pelvic examination.

Patient ran a slowly progressive downhill course with development of decubitus ulcers and loss of weight. There developed an increased spasticity with contractures of legs and, to a less extent of both arms. No changes in neurologic findings. Survived one mild pneumonic attack but quickly grew worse and died.

Clinical Impression.—Arteriosclerosis general and cerebral with hypertension; arteriosclerotic nephritis; optic atrophy; muscular atrophy and weakness with hyperactive reflexes, due to cerebral lesion, probably the result of vascular sclerosis; calcified uterine fibromas.

Autopsy Findings (Anatomical Diagnosis).—Generalized arteriosclerosis, especially of cerebral vessels; atrophy of cerebral cortex; encephalomalacia (corpus striatum); emphysema; lithopedion formation.

Upon opening the abdominal cavity a large firm calcified nodular mass presented itself in the midline just above the symphysis. At first glance the mass had the appearance of calcified fibroids. Upon further inspection however, fetal parts could be discerned. The uterus, tubes, and ovaries, together with the lithopedion, were removed and taken to the laboratory of Dr. J. Whitredge Williams, where further study was made. Dr. Williams kindly consented to describe the specimen.

DESCRIPTION OF LITHOPEDION

Radiographic Examination.—The head shows very little bone structure. It is covered by partially calcified folds which evidently represent remains of the fetal membranes. Dispersed throughout the surface of the specimen, there are several localized splotchy areas of calcification. The skeletal framework is quite well visualized and shows a rather marked kyphosis in the lower dorsal region. Two forked ribs are noted. The shafts of the long bones show localized areas of bone destruction and thickening of the cortex, to such an extent that in places it obliterates the medullary canals.

Macroscopic Examination.—The specimen consists of the pelvic viscera and the lithopedion. Upon dissecting off the bladder and lower part of the vagina, it is seen that the lithopedion lies to the left of and behind the uterus.

A frontal view shows that the uterus measures 7 cm. in length, and except for the presence of adhesions presents a normal appearance. The fundus presents the usual curvature and from the right cornu extend the senile right tube and ovary. The left cornu is elongated with its upper margin flattened out and in direct contact with the lithopedion, and from its outer end extends the left tube.

The lithopedion lies almost entirely to the left of the uterus with the compressed head lying below and the compressed body above the left cornu. The body is folded in such a way that the right knee rests upon and protrudes over the middle of the fundus, while the lower ends of both legs extend backwards and laterally beyond the right cornu. The head lies in close contact with the left margin of the uterus with its vertex below the level of the external os, so that in life, it must have depressed the vaginal fornix and Douglas' culdesac.

The posterior view of the specimen shows that the posterior wall of the uterus has been incised, that the entire organ is curved upon itself so that its left margin is concave and is closely applied to the right side of the fetal head. In this location, the posterior wall of the uterus and the tissues enclosing the lithopedion are continuous down to the level of the internal os, where the continuity ceases, and the head is separated from the uterine margin by a triangular space.

The left tube is 11 cm. in length and with the ovary, extends outward and downward over the head of the lithopedion to be attached to the posterior surface of the tissues covering the vertex, $1\frac{1}{2}$ cm. above its most dependent part. In its uterine portion, where it passes over a depression between the head and body of the lithopedion, the tube is flattened anteroposteriorly into a bandlike structure 2 or 3 mm. in thickness and 5 or 6 mm. in height. Laterally, it presents its usual tubular appearance and is 6 or 7 mm. in diameter. A definite fimbriated end is



Fig. 1.—Front view of lithopedion, showing relation to uterus, and adnexa.

lacking, and the outermost extremity of the tube is firmly attached to the tissues covering the head over an area of 10 by 3 mm. The left ovary is elongated, shows no adhesions, and measures 4 by 1.5 by 1 cm.

The right tube measures 6 cm. in length and 5 mm. at its thickest part. The fimbriated end is occluded, and it seems probable that it was distended in vivo. The right ovary is covered by adhesions, is atrophic and measures 2 by 1.5 by 1 cm. Over the upper part of the lithopedion are many adhesions, one of which, over the knees and lower legs, is clearly omental in character.

Gross examination makes it probable that we have to deal with secondary development within the left broad ligament, although the condition of the left tube speaks against such a view.

Microscopic Examination.—Sections were made from various points, in hope of learning details of the mode of origin, and whether any trace of placenta could be demonstrated.

Study of the sections is unsatisfactory for, while it apparently indicates that the fetus lies within the folds of the left broad ligament, it gives no information concerning the point of origin of the pregnancy, and nowhere shows any sign of placental tissue.

1. Shows typical uterine muscularis with unusual development of the intramuscular connective tissue and hyaline degeneration of many vessels. The endometrium is not as atrophic as one would expect, and, in addition to areas of pronounced epithelial desquamation, it presents numerous rounded and oval spaces, up to 3 mm. in diameter, lined by well preserved cylindrical epithelium.

2. Sections through median end of right tube and ovary show that the tube wall has its usual muscular structure, but that all trace of the mucosa has disappeared. Notwithstanding this, the lumen remains as a well marked slit, whose wall is made up of muscular and connective tissue. While the ovary is devoid of follicles, it still presents a characteristic structure, with well marked stroma, occasional corpora fibrosa and many hyaline vessels. There are signs of previous periophoritis, and areas of germinal epithelium may be distinguished beneath well formed connective tissue. Near its upper pole, the ovary contains an irregularly

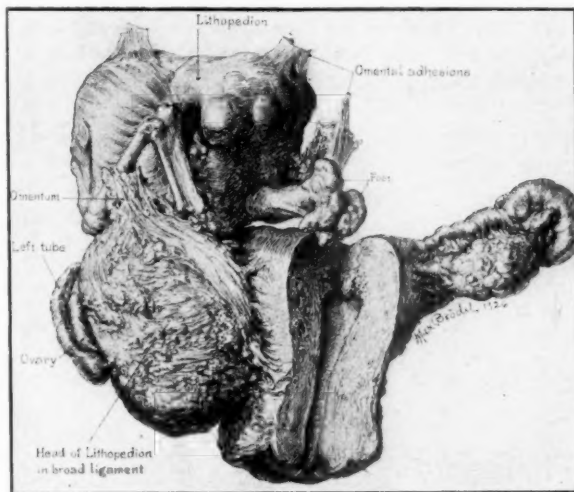


Fig. 2.—Back view of lithopedion.

rounded space, whose walls are irregular, and in places protrude into the lumen like a beginning papilloma. The cyst wall, as well as the projections, are covered by a single layer of cuboidal epithelium.

3. Sections through the median end of the left tube present the same structure as on the right side.

4. Except for its location, this section could not be taken for the ovary. It presents a capsule of muscular and connective tissue with many large vessels, while its interior is occupied by an oval mass 5 by 8 mm., which stains pink with eosin. Under the microscope, it consists of a structureless homogeneous tissue, which is almost devoid of cells, and the few which are present, are typical spindle-shaped connective tissue cells.

1835 EYE STREET, N. W.

AN UNUSUAL CASE OF ECTOPIC GESTATION

EDWARD G. WATERS, M.D., PH.B., F.A.C.S., JERSEY CITY, N. J.

(Attending Obstetrician, Christ Hospital; Associate Surgeon, Jersey City Hospital;
Attending Surgeon, Fairmont Hospital.)

MRS. M. U., aged twenty-nine, was seen in consultation with Dr. H. Schwarz, January 4, 1930. There was a history of a one-child sterility of nine years. Her husband was living and healthy. Of importance in her past history was a salpingitis, six years ago; no pregnancy since, no precautions used. She complained of recurrent lower abdominal pain and irregular bleeding. The last period was September 20, 1929, with onset of nausea in October, lasting two weeks. In November, the patient stained for four days and believed it a regular period, as she frequently missed one or two months. Early in December there occurred severe bilateral pelvic cramps and dull pains, associated with a heavy mucopuru-

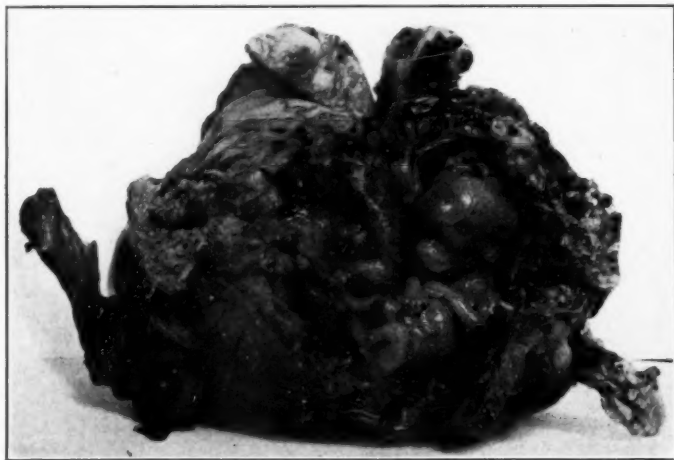


Fig. 1.—Left tube with fetus in situ, placental site bisected by incision.

lent leucorrhea. She was given a series of diathermy treatments, with some improvement. December 22, patient began to have crampy pains in left lower side, aching pains in legs, and passed a few clots. She bled heavily for two days, passed considerable detritus, and was believed to have miscarried. However, severe pains persisted, which were crampy and colicky in nature, and were felt over the entire lower abdomen, but were most marked in the left lower quadrant. There was considerable blood loss and progressive weakness. An ectopic pregnancy was considered and consultation requested.

The patient was in fair condition, apparently slightly anemic, markedly tender over the entire lower abdomen but slightly more so in the left hypogastric region. The uterus reached to within 2 fingers of the umbilicus. Vaginal examination revealed a vagina full of blood clots, a very soft, not tender, patulous cervix, and uterus enlarged to the size of a three months' or more pregnancy.

A semisolid mass, very tender and tense, about the size of an orange, occupied the left side of the pelvis, filling out the left fornix and giving marked pain on

bimanual pressure. The right adnexa could not be felt. It seemed inconceivable that a pregnancy would be retained from three to three and one-half months in the tube, especially after what seemed to be a miscarriage, in view of ergot and similar drugs administered. Also the size of the uterus was distinctly in favor of the diagnosis of incomplete abortion, complicated by ovarian cyst, with twisted pedicle, the latter presumably accounting for the miscarriage.

The patient was removed to the hospital. Spinal anesthesia was given and a curettage was performed. Large amounts of decidual tissue and what appeared to be the products of an incomplete abortion were removed from a uterus enlarged to that of a three months' size. A celiotomy was done and a large unruptured left ectopic pregnancy was found still bleeding through the fimbriated orifice of the intact tube. Large amounts of old and recent blood clots were found, with considerable free blood in the pelvis and abdomen. The fetus was about three months' size, the whole mass attaining the size of a large orange. It was removed in toto.

The right tube was found to be markedly thickened, enlarged and nodular, covered with old adhesions, and evidently the site of a former infection.

The unusual phases in this case are as follows:

1. The amount of external blood loss. It is decidedly unusual to have heavy vaginal bleeding with an ectopic pregnancy. The bleeding is scant, often a mere spotting, occasionally more. Few large clots are passed, and rarely is a decidual cast passed of sufficient size to resemble the aborted products of conception. In this instance not only was there a vaginal blood loss of dangerous degree, but passage of a large amount of formed detritus caused a diagnosis of miscarriage to be made.

2. The duration of the ectopic gestation. Usually only from four to eight weeks pass before tubal rupture takes place. Here, the pregnancy reached three and one-half months.

3. The uterine enlargement. The uterus always undergoes complementary enlargement in ectopic pregnancy, but rarely passes the size of a six weeks' pregnancy. Here the uterus was approximately the three and one-half months' size, it should have been were the pregnancy uterine.

4. The intraabdominal hemorrhage, which seemed quite extensive for fimbrial seepage with no actual tubal rupture. The size attained by the nonruptured tubal pregnancy, with the large chorionic surface facing the fimbriated end of the tube, accounts for it.

5. Pregnancy following a nine-year sterility, with gross and microscopic evidence of marked chronic tubal disease, again recalls the possibility of diseased tubes regaining patency.

REPORT OF CASE OF OVARIAN PREGNANCY

B. J. MOON, M.D., AND F. W. MULSOW, M.D., CEDAR RAPIDS, IOWA

MRS. L., aged thirty-four, married, housewife, has had four children, two alive and well, one stillbirth in 1923 and one died from peritonitis following a ruptured appendix.

In 1922 the patient had an appendectomy complicated with a pelvic peritonitis and made a good recovery in about three weeks.

Menstrual history was negative until present illness. The last regular menstrual period began November 23 with five days' duration which was her average time.

On December 7 she began to have a bloody vaginal discharge which required about one pad a day and complained of pain in lower portion of the back. Later in December about the time for her regular period the discharge increased in amount and was darker in color. About January 1 she began to have cramps across the lower abdomen which extended down into the rectum. The pain was not severe but would cause her to bend over and each attack would be about one hour in duration.

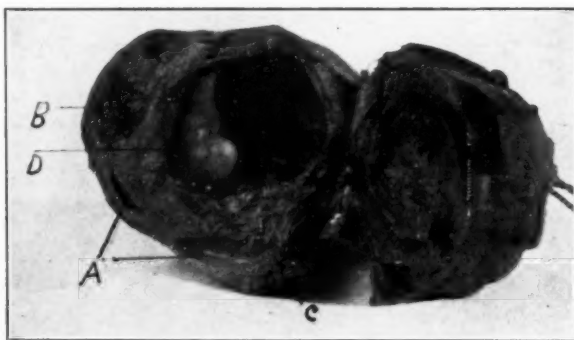


Fig. 1.—A, Cysts of the wall of the ovary, B, apparent corpus luteum tissue, C, piece of fimbriated end of tube, D, embryo.

She complained of weakness and soreness across the lower abdomen following each attack.

During one of these attacks a physician was called and after rest in bed for two weeks no more cramps occurred until about the last of January when the symptoms recurred. About this time, upon bimanual examination, there was a palpable mass in the right adnexa. On February 4, she had a severe attack of pain extending into the rectum. The pain was more severe than any previous attack and more vaginal bleeding occurred. The mass in the right adnexa had enlarged to about the size of a peach and was low and posterior to the uterus. It was well fixed and slightly tender. The white blood cell count was 6,000 and the urine was negative.

On February 5, she was operated upon; a preoperative diagnosis of ectopic pregnancy or cyst of right ovary, having been made.

Upon opening the abdomen a hemorrhagic mass was found to the right and posterior to the uterus. It was adherent to the rectum, and as it was released, blood clots were present between the rectum and the tumor mass. As adhesions from former pelvic peritonitis were released, the mass was found to be the right ovary. The ovary and tube was removed.

The patient made a normal recovery and was discharged from the hospital in fifteen days on February 20.

THE PATHOLOGIC FINDINGS

The ovary was dark red and somewhat pyramidal in shape. After being hardened in formalin it measured 7.5 by 6 by 5.5 cm. In the central region of the ovary was a cystic cavity 3 cm. across in which there was an embryo 2.3 cm. long. It was attached to the thinner portion of the ovarian wall, which was opposite to the point of attachment of the tube and ovarian ligament (Fig. 1). There was considerable hemorrhage and regions of softening in the wall.

The microscopic sections taken from several parts of the wall of the gestation sac showed the wall to be ovarian tissue. There were several small cysts in the wall. There was diffuse hemorrhage and many areas of degeneration. In the thick portion of the wall near the attachment of the ovarian ligament, there was what appeared to be coagulation necrosis of corpus luteum tissue, but this could not be definitely decided from many sections because of the degeneration. On the outer part of the wall near the ovarian ligament attachment was part of the fimbriated end of the tube. This tubal tissue did not extend through the wall to the fetal membranes. The chorionic villi are quite well preserved in most places. The tubal tissue was on the wall opposite the attachment of the embryo.

The embryo was definitely surrounded by ovarian tissue, yet there was some of the tube attached to the outer wall of the ovary. Impregnation might have occurred in the end of the tube but growth had taken place in the ovary, the location of the embryo was in the ovary.

In this case of ovarian pregnancy the embryo was quite well preserved. From the available literature, it appears that an embryo is found in about one-third of the cases of ovarian pregnancy.

HIGLEY BUILDING.

A REPORT OF A CASE OF HYDROPS UNIVERSALIS FETUS

BY CHARLES A. GORDON, M.D., F.A.C.S., BROOKLYN, NEW YORK

THIS case of general dropsy or hydrops universalis fetus is reported because of its rarity and the importance of adding postmortem examinations to the literature.

Brilliantly reviewed for the first time by J. W. Ballantyne in 1892, no such comprehensive study has appeared since, although E. A. Schumann, in 1915, reporting a case, reviewed the literature. He concluded that it is due to a maternal toxemia impairing the circulation and the nutritive function of the placental cells, and thereby causing secondary circulatory and nutritional defects to ensue in the fetus. No direct evidence, however, was adduced in support of this theory.

Well described by Ballantyne as "a very rare condition characterized by general anasarca, fluid effusions in the peritoneum, pleural and pericardial sacs, and usually edema of the placenta, it usually results in death of the fetus before, during, or immediately after birth." It is to be distinguished from edema neonatorum, congenital elephantiasis, fetal syphilis, ascites, and fetal peritonitis.

L. S., Italian, seen by me with Dr. Chiaramonte, entered St. Catherine's Hospital, on January 15, 1931, in labor. She was twenty-nine years old, and had had

three children, all born spontaneously. The first is eight years old, the second died of jaundice one month after birth, and the third was stillborn at the eighth month, cause unknown. Her past history and also her husband's were negative for any familial disease or serious illness.

The duration of her pregnancy was thirty weeks. The antepartum period had been uneventful until the twentieth week when her abdomen began to grow rapidly in size with steadily increasing distress, and later pain and dyspnea. She felt life but little, with only occasional sluggish fetal movements.

When she went into premature labor, her abdomen was tense and markedly distended; the fetal heart sounds were even but distant, and fetal parts were not palpable. Pelvic measurements were normal. Her blood Wassermann, as well as her husband's, was negative. Labor progressed steadily. After eight hours, when the cervix was fully dilated, the membranes ruptured and a large amount of fluid escaped. The second stage lasted three hours, and was characterized by such violent, almost tonic uterine contractions, with the vertex at the spines, that uterine rupture seemed imminent. Delivery, however, was noninstrumental under light anesthesia and spontaneous to the shoulders. The fetal abdomen so distended the birth canal that strong traction was necessary. The fetus did not breathe, but heart action was visible for a few minutes. The placenta separated rapidly and was then easily expressed, notwithstanding its great size. The puerperium was afebrile and uneventful, and the patient was discharged in eleven days.

Pathologic Report.—Necropsy of newborn infant by Dr. E. H. Nidish. Female fetus measuring 43 cm., weighing 3980 gm. The skin was glossy, of a deep pink color, with deep markings at the flexures of the limbs. Surface edema was general except in the feet, which were very small. It was most marked in the buttocks and forehead, completely closing the eyes, and pitting 2 cm. deep could easily be obtained. There were no bodily deformities and no maceration.

The circumference of the abdomen was four and a half times the diameter of the head, the peritoneal cavity containing 1000 c.c. of clear straw-colored fluid. The liver was large, and under its left lobe posteriorly were found closely packed nonadherent coils of small intestine. There was very little meconium in the large intestine. The gall bladder was normal and contained some bile. The spleen was two and a half times its normal size, soft and quadrangular. The urachus and umbilical vessels were normal, as well as the pancreas, uterus, adnexa, and genitourinary tract.

The entire thorax, with its viscera, was displaced upward. The lungs were small and unexpanded and both pleural cavities were filled with fluid. The heart was small, but normal, with patent ductus arteriosus, and the pericardial sac was also distended with fluid.

The bones of the skull were well ossified, but the skull was not opened.

Microscopic examination of kidney, liver, spleen, and pancreas revealed nothing but marked anemia.

The placenta weighed 2064 gm., measured 10½ by 9 inches, and was over two inches in thickness. It was markedly edematous, friable, and pale. On section large quantities of fluid escaped. Histologically, it showed great edema with swollen and degenerated syncytial cells. Many villi were necrotic. The cord was almost three inches in circumference and also showed marked edema.

A PERINEAL RETRACTOR IN BREECH DELIVERIES*

ROBERT E. SEIBELS, M.D., F.A.C.S., COLUMBIA, S. C.

BREECH deliveries in primiparae, and often in elderly multiparae, remain one of the major problems in obstetrics. To most of us this presentation offers difficulties which occasionally are of extreme degree. Except in the hands of the most expert, there occurs extension of the arms, nuchal hitch, and extension of the head sufficiently often to arrest our enthusiasm and to give the obstetrician cause for serious thought when faced with this type of delivery.

After we have successfully overcome the above mentioned difficulties, there remains the protection of the maternal soft parts and the prevention of fetal asphyxia from inspiration of amniotic fluid and blood. It has been clearly demonstrated by Potter and his followers that the necessity for hurry, formerly taught, between the birth of the navel and the mouth does not exist, and it has also been clearly demonstrated that if we are extremely gentle in making traction on the baby's body, allowing it to be born largely by maternal effort, there will be no attempts at respiration on the part of the infant. Strong traction on the feet, extending the trunk, depresses the diaphragm and fluid is mechanically drawn into the baby's lungs. That one can be deliberate and obtain better results by not performing traction on the legs and trunk we have often demonstrated to our satisfaction and have frequently allowed twenty minutes to elapse between the birth of the navel and of the mouth. True as we know this to be, each minute that elapses from the time the umbilicus appears seems interminable, and we find the greatest difficulty in not hurrying the procedure from then on.

Especially do we feel the urge for speed when the shoulders have been successfully delivered and the hand, passing along the baby's throat finds the mouth free of the cervix, lying in the hollow of the sacrum. From this time on, it is nearly impossible to restrain one's energy and enthusiasm so that excess pressure is often made on the baby's head, shoulders are dragged on and even forceps have been devised rapidly to extract the head through the comparatively undilated vagina. One has only to review a series of such deliveries in his own practice to recall instances where he wrought serious damage either to the baby or to the maternal soft parts, or both, by hurrying this portion of the delivery. When the breech follows a version and the baby has had the maximum amount of stimulation to respiration from handling, the accoucheur is especially liable to feel a necessity for speedy delivery.

About five years ago, we began to consider the problem of fetal

*Read before the Eastern Carolina Medical Association, Myrtle Beach, South Carolina, July 23, 1931.

asphyxia after a series of disasters. If we could empty the upper respiratory passages of accumulated fluid and get air to the baby so that it could breathe when the mouth is free of the cervix, we would then be more content to let the delivery progress in a normal, slow manner, simply aiding maternal efforts in expulsion by moderate pressure on the fetal occiput. At first, we passed a catheter to the mouth and endeavored to empty the throat by suction and permit respiration, but with indifferent success. However, in attempting to pass the catheter on one occasion, it occurred to us to use a Sims retractor in order to depress the perineum and pass the catheter by sight rather than by touch. When the retractor was inserted and the perineum depressed, the baby's mouth was clearly exposed although it lay well above the ischial spines. Fluid was easily massaged from the throat and the baby began to breathe at once. The necessity for the catheter had been eliminated and since then we have used a perineal retractor as a routine procedure as soon as the chin passes the cervix.

The Sims retractor offers certain disadvantages which quickly became apparent and the malleable ribbon retractor was substituted for it. This retractor can be readily bent to any shape and length of blade desired and is more easily held by an assistant. As soon as the mouth is exposed by the retractor, the fluid is removed by sponges, the baby's body being held in slight extension at the neck. The throat is massaged gently and emptied and the baby begins to breathe. With the retractor in place, and the baby breathing, full protection can be offered to the maternal soft parts and the rapidity of the remainder of the delivery can be governed entirely by the mother's condition rather than by the fear of fetal asphyxia. The retractor is gradually withdrawn in front of the advancing brow and is removed as the mouth is born. Since its routine use, we have not had occasion to apply forceps to the after-coming head and there has been a decided lessening in damage to the musculature of the vaginal outlet. Occasionally faced with the necessity for performing a breech delivery without adequate assistance, the weighted vaginal speculum of the Edebohls type has been used, though not as efficiently as the ribbon retractor in the hands of an intelligent assistant. A search of the literature has not so far revealed previous recommendation of this method.

THE MEDICAL BUILDING

IMPROVED RECEIVING TABLE FOR THE NEWBORN

By HARRY STUCKERT, M.D., F.A.C.S., PHILADELPHIA, PA.

AFTER completion of the second stage of labor, not infrequently considerable time is required for the resuscitation of the baby, the ligation of the cord, and the institution of prophylactic treatment for ophthalmia neonatorum.

The temperature of the delivery room (80°) being much lower than the intra-uterine (100°) exposes the newborn to shock and pulmonary complications if kept in the low temperature for any length of time.

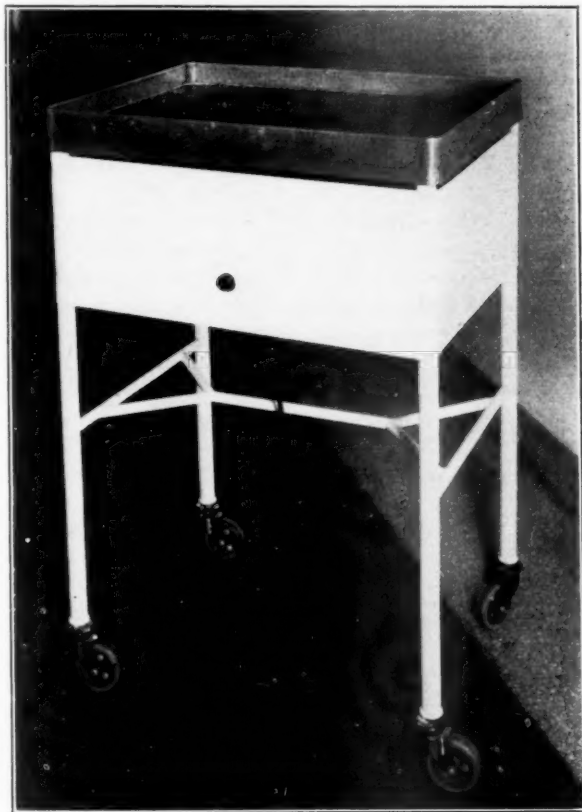


Fig. 1.

In order to maintain the body temperature and aid in the reduction of early complications occurring in the newborn from exposure to the sudden change in temperature, I have devised a method whereby the receiving table can be heated.

It consists of the small side table used in the operating room, the upper portion of which is inclosed. A series of electric light bulbs is placed within the inclosure.

The receiving surface of the table can be heated within five minutes and different degrees of temperature can be obtained by the attached three-way switch control.

This table is being used in the delivery rooms of the Jefferson Medical College Hospital.

248 SOUTH TWENTY-FIRST STREET

A REPORT OF A CASE OF CHORIONEPITHELIOMA FOLLOWED BY THE FRIEDMAN TEST

MAXWELL E. LAPHAM, M.D., PHILADELPHIA, PA.

(From the Department of Gynecology of the Hospital of the University of Pennsylvania)

MRS. E. P., para iii, all spontaneous deliveries; last pregnancy in 1928. Last menstrual period November 16, 1930. On February 27, 1931, the patient reported to the dispensary with the complaint of spotting during the previous week. At that time, she had no other symptoms except anorexia and general weakness. After continuing to bleed for another week, she was admitted to the hospital. On March 7, 1931, a pelvic examination showed a soft cervix, moderate sanguineous discharge, a fundus the size of a three months' pregnancy. After rest in bed for five days, the bleeding ceased and the pelvic findings remained the same in other respects. The patient at that time gave a positive Friedman reaction. She was told to report to the hospital frequently for observation and to report immediately if there were any more bleeding.

On March 14, she returned bleeding moderately; this did not cease after the patient had been kept in bed for several days. The uterus had not increased in size and was slightly smaller than it should have been according to her menstrual history. It was concluded that the patient had an inevitable abortion, perhaps a missed abortion because of the apparent failure of the uterus to enlarge. She had a moderate anemia, hemaglobin 60 per cent, and it was decided to evacuate the uterus. A pregnancy test was not done at this time.

On March 17, the uterus was evacuated. No fetal parts were found but a great quantity of "decidual" tissue was removed. Several pieces of this tissue were rather typical of the "grape-like" formation of a hydatidiform mole. The pathologic examination verified the operative diagnosis. The patient made an uneventful recovery and at the end of ten days was discharged, having no bleeding, and with a uterus fairly well involuted, in a posterior position but freely movable and easily replaced.

On April 24, about one month after her second discharge from the hospital, she returned with the report that she had bled two days previously. The fundus was found to be slightly larger than normal and freely movable, and she had a profuse leucorrhea. A Friedman test was done and found to be positive, so that a second intrauterine examination was made and the pathologic report of the curettings showed the presence of chorionepithelioma.

On May 12, a panhysterectomy and bilateral salpingo-oophorectomy were done. Upon examination of the uterus grossly, it showed rather a discrete mass elevated above the endometrium. It was about the size of an egg and was situated on the posterior surface of the uterine cavity. The external surface of the uterus was smooth and pink. Upon microscopic examination, the tumor had penetrated into the myometrium but not through it. The tubes and ovaries were negative. The patient made a very good ultimate recovery and left the hospital on May 31, 1931.

On June 29, the patient again returned complaining of general weakness, deafness in the left ear and precordial pain. A pelvic examination revealed slight tenderness but no more than the normal amount after such an operation as the patient had undergone. She was destitute and apparently had been getting very little to eat, so that her general weakness and other symptoms might have been

due to malnutrition. She was extremely underweight and her blood pressure very low. A Friedman test done at this time, one month after operation, proved to be negative.

On September 4, the Friedman test was repeated and again was negative. The patient, in the meantime, had been living under better conditions and had gained weight, appearing and feeling much improved. Her only complaint was of a rather constant backache. Four months after operation, the patient was in fairly good health, and one would assume that she had made a complete recovery.

There are about 42 cases of hydatidiform mole reported to have been diagnosed and followed by the Aschheim-Zondek test or the Friedman test. Nearly as many cases of chorionepithelioma have been followed in the same manner, and the progress noted, by one of the two tests.

Schultze in Germany reported a case of chorionepithelioma which gave a positive Aschheim-Zondek reaction after hysterectomy. Metastases were found in the lungs by x-ray. Under irradiation, the patient recovered and the Aschheim-Zondek test became negative.

Otto has reported a case of ruptured chorionepithelioma, and after hysterectomy metastatic lesions were found in the lungs. Until death, three weeks after operation, the Aschheim-Zondek test remained positive.

Gerritgen reports a case of hysterectomy for chorionepithelioma followed for ten weeks after operation by the Aschheim-Zondek test, which always was positive. At autopsy, it was revealed there were metastases in the lungs and liver.

I have only mentioned a few of the cases in the literature in an attempt to show the importance of a careful "follow-up" of this type of case. It would seem that the Aschheim-Zondek and Friedman tests are extremely valuable in the diagnosis and prognosis of cases of hydatidiform mole and chorionepithelioma.

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(For discussion, see page 911.)

Erratum

In the Dieckmann and Wegner article, in the May number, the legend for Fig. 4, page 662, should read: "Fig. 4. Kidney. Shows the convoluted tubules in a state of *albuminous degeneration*." instead of hyaline degeneration.

Society Transactions

NEW YORK OBSTETRICAL SOCIETY

MEETING OF OCTOBER 13, 1931

DR. N. B. SACKETT (by invitation) presented a paper entitled **Intra-peritoneal Hemorrhage of Ovarian Origin**. (For original article see page 849.)

DISCUSSION

DR. R. T. FRANK.—It is quite evident that there is no single cause for ovarian hemorrhage. I agree that probably exaggeration of physiologic congestion near the time of menstruation plus some trauma or other cause which varies and cannot be readily found in the individual case, must be the explanation. We may have spontaneous hemorrhages anywhere in the body at this time. The ovary is well protected and yet a case was reported of a young girl who jumped over a fence and in doing so apparently, as was shown at operation, tore the ovarian cortex, causing intraperitoneal hemorrhage which manifested itself shortly after. A careful study of each individual case is indicated.

DR. G. G. WARD.—I agree likewise that it is extremely difficult to find any one factor, when so many things may cause rupture. The physiologic conditions are such that bleeding from the ovary is easy. There is no doubt that trauma is a factor. The point, of course, of great interest is the differential diagnosis from ectopic gestation and other conditions.

DR. GEORGE GELLHORN read (by invitation) a paper entitled **Local Anesthesia in Gynecology and Obstetrics**, of which an abstract follows.

Although local anesthesia by means of infiltration is unquestionably the least dangerous of all methods of surgical analgesia, it has, among gynecologists, not yet attained the popularity which it enjoys in the field of general surgery. It is true that gynecologic laparotomies can be performed under local anesthesia with ease and dispatch only when the operative technic and the operating room personnel are, so to speak, attuned to it. As such favorable conditions do not prevail in a general hospital, the author has used local anesthesia in abdominal operations only in very exceptional cases. In vaginal operations, on the other hand, local anesthesia enters into the closest competition with other means of relieving pain and, in fact, becomes the method of choice. The operations concerned fall into two large groups, namely, first, those on the uterus (dilatation and curettage, cervical amputation, anterior hysterotomy, interposition, hysterectomy, morcellation of fibroids), and, second, those on the outer genitals (partial or total vulvectomy, anterior colporrhaphy, perineorrhaphy, repair of complete tears). In the first group analgesia is produced by infiltration of the parametria, in the second by infiltration of the field of operation. The details of the technic have been discussed by the author in two previous papers in *Surgery, Gynecology and Obstetrics* in 1927 and 1930.

The standard fluid for injection is a $\frac{1}{4}$ per cent novocaine in a normal saline solution with the addition of 3 drops of adrenalin to each ounce of the fluid. In

every case, the patient is brought to the operating room in a fairly deep "twilight sleep" so as to allay her apprehension and to render the unnatural lithotomy position on the operating table endurable. In the vast majority of instances, complete analgesia is accomplished within five minutes and maintained throughout the operation; very rarely is a whiff or two of ether or gas required in lengthy operation, chiefly to relieve the discomfort of the strained posture. The amount of fluid needed ranges, according to the nature of the operation, from 2 to 4 ounces. Since the low percentage of the novocaine leaves the solution practically isotonic, there is no danger of toxicity even when large amounts have been used. Neither has the infiltration in hundreds of cases and in more than ten years ever interfered with wound healing. On the other hand, it has rendered operating completely bloodless in most instances and made dissection easier where such was required.

There are only two possible dangers connected with this method which, however, may readily be prevented. The needle may enter a blood vessel. In this case, the novocaine solution would be injected directly into the circulation and this would cause alarming symptoms. Although this complication has proved to be of short duration in the very few instances reported in literature, it may be avoided by a tentative pull on the piston which would show the absence of blood in the syringe. The second possible danger may come from breakage of the needle. Steel needles rust easily, and if a break occurs it is near the hub. The simple precaution consists in not inserting the needle its entire length.

Compared with these few negligible complications, the advantages of local anesthesia are numerous and impressive. Undisturbed by bleeding and no longer forced to work at top speed, the tissues involved can be carefully dissected and approximated. Further, all vaginal operations are more readily borne by patients than abdominal ones. This advantage is even more apparent when we are dealing with unfavorable cases, so-called "poor surgical risks." In this category we must first place aged people. The oldest patient on whom the author performed a vaginal hysterectomy under local anesthesia with perfect success, was seventy-six years of age. The author has operated successfully upon a number of patients with active tuberculosis, diffuse bronchitis, emphysema, cardiorenal disease, diabetes, and exophthalmic goiter. Neither hypertension nor hypotension form contraindications, as systematic blood pressure readings during operations have revealed no effect of local anesthesia in either direction.

In the field of obstetrics local anesthesia is more widely used in cesarean section. As a matter of historical interest it should be noted that the first operation of this sort was performed by Webster in Chicago in 1909. The author prefers the low cervical section and, as a rule, uses local anesthesia only for incising the abdominal wall. The separation of the bladder, the incision into the lower uterine segment and extraction of the child are done under a short ethylene narcosis, but the repair of the uterus and closure of the abdominal incision require no general anesthesia. It is, however, freely admitted that many other operators perform this operation entirely under local anesthesia. In any case, the traditional haste in closing the uterus becomes unnecessary and the increased thoroughness of adaptation acts as a safeguard against future rupture.

Of other obstetric operations, curettage for incomplete abortion (which, however, often requires nothing more than "twilight"), and interruption of pregnancy by means of anterior hysterotomy may be mentioned. In a recent case of the last named kind the patient suffered from a severe uncompensated heart lesion but passed easily through the operation during which she had no loss of blood whatever.

The use of local anesthesia in normal deliveries seems to the author of great practical value. The patient receives a preliminary semianesthesia by means of

morphine and scopolamine, amytal, or the like, which lasts well into the second stage. When the head descends below the spines, the lower circumference of the vulva, the levators and the perineal body are well infiltrated. This is followed within a few minutes by a marked relaxation of the pelvic floor, and the head passes painlessly either spontaneously or with low forceps through the vulva. Local anesthesia at this stage almost invariably slows down uterine contractions, and for this reason an injection of pituitrin is desirable. It has, of course, no ill effect on the child and none on the course of the third stage. Episiotomies can be made and, later, repaired without loss of blood or sense of pain, and the same is true of any tears that may have occurred. There is about local anesthesia in normal deliveries a sense of security and a simplicity and ease which render the procedure applicable both to hospital and home obstetrics, and in the latter case obviate the need of an anesthetist. The advantages of local anesthesia are accentuated when we have to deal with complicating diseases which render the use of inhalation narcosis undesirable. In this connection the author refers to cases of diabetes, acute bronchopneumonia, tuberculosis, and heart disease in which he employed local anesthesia with satisfaction.

With all these points in its favor, local anesthesia however, has its limitations. It cannot well be used in patients so nervous and apprehensive that even the preliminary "twilight sleep" fails to allay their restlessness. There are other patients who have an idiosyncrasy against novocaine even in the small amount used, and others in whom, for unexplained reasons, analgesia cannot be accomplished. In gynecologic operations where extensive peritoneal adhesions are encountered, local infiltration cannot do away with the pull on the parietal peritoneum and the resulting pain. In such instances, general narcosis may have to be instituted for a short time or the entire length of the operation. At any rate, no claim should be made for local anesthesia being a cure-all, but the advantages and the safety of this method are so great that they deserve earnest consideration in the field of gynecologic and obstetric surgery.

DISCUSSION

DR. A. C. BECK.—I would like to ask if veronal may be given the night before and the morning of the operation, in addition to the morphine and scopolamine.

DR. I. C. RUBIN.—My experience with local analgesia in obstetrics began about eight years ago in a case of pulmonary tuberculosis, both apices being cavernous. Several months preceding her delivery she had a tuberculous involvement of the larynx. One of the measures used consisted not only in keeping her absolutely quiet, but absolutely silent. As cesarean section appeared ideally indicated, I resorted for the first time to the use of local analgesia. The patient made a perfectly uneventful recovery. In that case I used gas while closing the abdominal wound. Since then, I have had a number of occasions to use local anesthesia in cesarean section. Its greatest advantage, as Dr. Williamson mentioned, is the almost negligible loss of blood. The uterine wall is blanched, the contractile power of the uterus appears to be not only retained, but it is increased.

I have also had occasion to use local infiltration for dilatation and curettage successfully at the Mount Sinai Hospital. The only painful reaction is encountered in dilating the internal os. The curettage itself is painless. If one infiltrates the parametrium carefully and sufficiently, pain may be averted; the cervical os dilates easily and there is no pain.

In gynecology I have found it valuable in those instances where the use of a general anesthetic is contraindicated, and where an expert in paravertebral anesthesia is not available. Another advantage of local anesthesia is the facility it affords in separating planes of cleavage, making the operation very much simpler.

OBSTETRICAL SOCIETY OF PHILADELPHIA

MEETING OF OCTOBER 1, 1931

DR. MAXWELL LAPHAM reported **A Case of Chorionepithelioma Followed by the Friedman Test.** (For original article see page 906.)

DISCUSSION

DR. JACOB WALKER.—A few months ago I was called to see a patient who was supposed to be threatened with abortion, but finding the uterus entirely out of proportion to the supposed time of pregnancy, I suspected a hydatidiform mole. I emptied the uterus and it proved to be this condition. She began to bleed shortly after she got home, and I had a Friedman pregnancy test performed which proved positive.

About ten days later I had the test repeated, it proved strongly positive. With these findings, I became suspicious of the development of chorionepithelioma. I went one step further, and had the Groskin test for malignancy and it proved positive.

With all these positive findings, I advised the patient to be operated upon. I then lost track of the patient but found that she had gone to another doctor, and after a period of time the hormone tests became negative.

I wish to bring out the fact that if the Friedman tests are of any assistance in the diagnosis of chorionepithelioma, the urine used in the test would have to be one-fifth strength of the normal urine, because chorionepithelioma gives a marked reaction, practically five times the strength of the normal urine of pregnant women.

DR. LAPHAM (closing).—I am doubtful about the use of one-fifth strength urine in the Friedman test. I believe that in the Aschheim-Zondek test the titration is about in that proportion, and that the reaction is five times as strong in chorionepithelioma as in normal pregnancy. However, in talking to Dr. Friedman he said that according to tests he had been working on, the titration in the rabbit cannot be compared with that used in rats, and he still felt uncertain about this matter until further work had been done.

DR. CHARLES C. NORRIS AND DR. DOUGLAS P. MURPHY presented a paper entitled **Malignant Ovarian Neoplasms.** (For original article see page 833.)

DISCUSSION

DR. WILLIAM R. NICHOLSON.—This paper emphasizes the fact that every case of real ovarian disease should be operated upon. The import of an ovarian tumor is much more threatening than fibroids for instance, and demands much more prompt operative treatment than does the latter condition. Another thing to be emphasized is that every case in which definite disease suggesting malignancy is found in one ovary at operation that the other ovary should always be removed.

With regard to Dr. Norris' statistics I feel that the mortality should be corrected, for there is no reason to include as malignant deaths, those women who died so soon after operation that the shock of the operation itself was probably the cause.

With regard to the x-ray, either before or after operation, I am still uncertain. My present belief is that it should be used in the vast majority of cases operated upon, while I am not convinced as yet as to its actual value.

DR. CHARLES A. BEHNEY.—Regarding the use of x-ray therapy in the treatment of ovarian malignancy, distinction must be made between the x-ray therapy practiced eight or ten years ago, and the high voltage treatment of the present time.

I have seen a number of patients who have had recurrences treated by high voltage irradiation. While none of these recovered completely, it is not unusual to note regression of the growth over periods varying from three to eight or nine months. This would indicate that the therapy is of real value.

X-ray therapy has improved, not only in respect to the penetrability of the rays, but also with regard to the precision of their dosage and cross-fire. Results obtained with modern apparatus, efficiently operated are not to be compared with the former soft-ray therapy administered in "hit or miss" manner. Recurrences can be prevented by high voltage therapy given immediately after operation, better than destroyed after they have developed.

DR. BROOKE M. ANSPACH.—It has always seemed to me that cancer of the ovary was much more uniformly fatal than cancer of the uterus. Unfortunately we have no statistics relative to ovarian cancer compiled with the same care that is observed in the reports or the treatment of uterine cancer; therefore there is no accurate basis of comparison.

The high death rate probably depends to a considerable extent, I believe, upon the fact that most ovarian cancers are diagnosed late. In our experience the majority have a palpable tumor, so recognized by the patient before they seek medical advice. In carefully studying the history, it appears that abdominal pain has been present for a considerable time before the patient has noted the abdominal enlargement but the pain has been of such a moderate degree that it has been disregarded. It may be thought by the patient to be intestinal indigestion or it may be referred to the bladder (irritability and distress attending urination) or to the rectum (difficulty or pain with defecation).

Sometimes the first symptom of ovarian carcinoma is bleeding. At an early stage there may be no palpable uterine enlargement, the woman often being very fat. Under these circumstances, after a negative diagnostic curettage, it is a great temptation to apply radium to the inside of the uterus. We have had at least one case in which such an application had been made the real nature of the trouble not appearing until later. Accordingly it would appear wise, in cases of postmenopausal bleeding, where the uterus is not enlarged and the mucosa shows nothing malignant, to delay the use of radium until a sufficiently long period of observation has ruled out the probability of an ovarian cancer.

DRS. JOHN A. McGLINN and STEPHEN E. TRACY also discussed this paper.

DRS. FLOYD E. KEENE AND ROBERT A. KIMBROUGH presented a paper entitled **End-Results of Radium Therapy in Carcinoma of the Cervix.** (For original article see page 838.)

DISCUSSION

DR. BROOKE M. ANSPACH.—The paper of Drs. Keene and Kimbrough forms the basis of an interesting comparison between the results they have had at the University Hospital and the results that Drs. Scheffey and Thudium reported last year from the Jefferson Hospital. The percentage of salvages was about the same, 15 per cent.

We have used nearly the same technic. In the earlier part of our series the dose was 2400 mg. hours, whereas in some of the later cases we increased it up to 3000 to 3600 mg. hours. Our idea in the beginning was that the first dose should be the maximum one and that irradiation should not be repeated. This probably grew out of the fact that in the beginning of our use of radium the effect at the end of six weeks was so striking that one was tempted to repeat the treatment at once. Almost invariably the second irradiation changed a patient free of symptoms to one with

many of them. In other words the second irradiation seemed to undo the relief of symptoms accomplished by the first application. In the course of time, however, although the initial dose has been slightly increased, we have reirradiated, but only where there was a visible occurrence of the carcinoma, in a position where irradiation was possible without injury to the surrounding tissues.

It is interesting to note one patient who through some error was given 1200 mg. hours in the beginning and six months later 3000 mg. hours; she is still living and well after eight years.

We have not used high amputation with the cautery knife. In the early stages we carefully avoid curettage or even any disturbance of proliferating carcinomatous masses: in later years, however, we have removed most of the redundant part with a cautery knife, taking great care to avoid anything like curettage.

In regard to a larger dose, in our experience 3600 mg. hours seems to be the safe limit. Any dose higher than that must be used with great caution as fistulae may follow no matter how careful the radium is screened. We have had two cases with very far advanced carcinoma in which the use of a large dose of radium, 3600 to 4000 mg. hours, was fatal. In one, an unsuspected pyosalpinx was the cause of a peritonitis; in the other nothing was found at autopsy so that we concluded that she had died from a toxemia, the result of absorption from the irradiated cancer tissue.

In the group of cases that we reported, it is interesting to note that two of our five-year recoveries were of the squamous cell type or the type usually resistant to radiotherapy.

Although very few of the cases in our reported first series were treated with the x-ray subsequent to radium, at the present time we believe, that deep x-ray therapy should be used as a rule, and in very advanced cases, before irradiation with radium. In the individual case of cancer of the cervix a very thorough anatomical study of its growth will help us reach a wise decision as to the dose of radium, the screening, and the exact distribution of the radium in the affected areas.

DR. STEPHEN E. TRACY.—It was a surprise to note that in the 479 cases seen by Keene and Kimbrough, 58, or 12 per cent, of the cases were in Group 1. In most clinics, the truly early cases do not constitute more than 2 per cent of the cases. The high percentage of cases in Group 1 is probably one explanation of their low percentage of five year cures.

The results from any method of treatment of carcinoma in any part of the body, will not be improved to any extent until the public and the profession are educated to the importance of early recognition and the advantage derived from prompt and appropriate treatment. No method of therapy will ever cure a patient afflicted with carcinomas, who comes for treatment in the terminal stage. During the last year, the Group 1 cases of carcinoma of the cervix uteri treated with radium as reported from a few clinics, show 100 per cent of five-year cures.

The number of milligram hours of radium given at a treatment does not mean anything. It is a question of filtration. We are gradually working over to larger dosage with heavier filtration, and the radium treatments are followed by deep x-ray therapy.

DR. CHARLES A. BEHNEY.—Recently at the Philadelphia General Hospital, in order to evaluate the use of deep x-ray therapy, we studied cases that had died since the institution of the Radium Clinic, and found that the duration of life was longer in Stage 3 cases, who received high voltage x-rays in addition to radium. On the other hand, in 186 cases in Stage 4, the patients who received deep x-ray therapy alone lived three times as long as those who received radium alone.

DR. DANIEL LONGAKER.—There is one point in this discussion that ought to be added to make it complete, and that is the very great responsibility of the fam-

ily doctor and the obstetrician in the matter of early diagnosis of carcinoma. The importance of postnatal care cannot be too strongly emphasized and every one who has an obstetric clientele should strive to train himself to recognize all departures from the norm, not only abnormality to touch but abnormality to sight under correct illumination with proper speculum exposure. No parturient should be discharged until she is well locally and generally.

DR. KIMBROUGH (concluding).—This series of cases has not been analyzed from the standpoint of the age of the patients, in whom the best results were obtained. Such an analysis, however, was made by Dr. Norris and myself in 1926 in 263 cases, and we found that the best results were obtained between the ages of forty and fifty years.

DR. F. E. KEENE AND DR. F. L. PAYNE presented a paper entitled **The Investigation of Sterility**. (For original article see page 857.)

DISCUSSION

DR. CHARLES MAZER.—We must not minimize the importance of the Hühner test in the study of sterility. Hostility of the cervical secretions in women who show no evidence of cervical infection is, in my opinion, indicative of an endocrine factor which, when removed, usually results in a positive Hühner test.

Doctors Keene and Payne stressed the importance of the Frank and Goldberger test in the diagnosis of sterility in regularly menstruating women who present no pelvic pathology and whose mates are normal. Women who fail to show a normal premenstrual level of female sex hormone in the circulating blood almost invariably show a lack of nidatory changes when curetted a day or two before the expected onset of the flow. As the corpus luteum, through its dual secretion, is simultaneously responsible for the premenstrual high level of female sex hormone and the nidatory changes in the endometrium, the absence of one or both may be taken as evidence of faulty luteinization without disturbance in the menstrual rhythm.

We have three drugs at our disposal which are of some value in the treatment of menstrual disturbances and the associated sterility. The two conditions merge insensibly.

Thyroid extract has no specific action. It accelerates cellular activity in every organ, not excepting the endocrine system. A marked diminution of thyroid function may profoundly affect the sex glands, but the condition is comparatively rare.

The anterior pituitary sex hormone, upon which ovarian function depends, is now available for therapeutic use. Dosage of this hormone is still undetermined. The administration of 50 M.U., hypodermically every other day, has given me encouraging results.

The standardized female sex hormone has no stimulative action upon the ovaries. It does, however, produce growth and vascularity of the uterus and renders it more responsive to whatever ovarian function there may be present or to renewed ovarian function as a result of treatment directed to the pituitary and ovaries.

The best results are obtainable through the use of low-dosage irradiation of the pituitary and ovaries.

DR. JACOB HOFFMAN.—We have been using the Frank and Goldberger female sex hormone test and the anterior pituitary hormone tests for the determination of ovarian activity on Dr. Anspach's service at Jefferson Hospital, and find them of value in estimating ovarian function. There are cases, however, in which the female sex hormone test tends to be misleading, as, for example, in amenorrhea accompanying follicular atresia and in menstrual disturbances during the early menopause. In these cases, a polyfolliculin stadium is often present, a result, we believe, of the absence of corpus luteum formation. Lacking the inhibitory control of the corpus

luteum, there follows the successive formation of atretic follicles and retention cysts, with a resulting accumulation of follicular hormone. This condition usually leads to a hyperplasia of the endometrium, and the female sex hormone test, in such cases, not infrequently shows large amounts of this hormone in the blood, despite the fact that we are dealing with a hypo-ovarian state. This test has proved reliable where it has yielded a negative reaction. In the latter class of cases it may be taken as an index of follicular insufficiency.

Concerning the anterior pituitary hormone tests, a positive reaction may safely be considered as indicative of ovarian failure.

In our experience, the most important and reliable, as well as the most valuable aid in estimating ovarian activity is the histologic picture of the endometrium presented by the curettings taken just before the expected period. A premenstrual endometrium found at this time may be taken as a sign of intact ovarian function, and of the presence of the follicular and corpus luteum hormones in the proper proportion. An atrophic endometrium signifies follicular inactivity and a deficiency of the follicular hormone. A hyperplastic endometrium shows an excess of the follicular hormone and a deficiency of progestin, the hormone from the corpus luteum.

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D., ASSOCIATE EDITOR

Collective Review

A Critical Review of the Obstetric Literature of 1931

J. P. GREENHILL, M.D., CHICAGO, ILL.

(Concluded from May issue.)

LABOR

General.—In an elaborate series of experiments on dogs Rudolph and Ivy⁹⁵ studied the coordination of the uterus in labor and found that there is both an intrinsic and an extrinsic coordinating mechanism and one may subserve, in part at least, the function of the other. Ivy, Hartman and Koff⁹⁶ record for the first time the manner in which the wave of contraction passes over the parturient uterus simplex of the monkey. From a constantly quiescent area slightly ventral and cranial to the insertion of the tubes, elliptical, concentric waves of contraction pass medially in the midline and cranial border of the uterus progressing caudally then involving the lower uterine segment and finally the cervix. (These interesting experiments will undoubtedly shed a great deal of light on such obstetric problems as so-called uterine atony, irregular uterine contractions, tetanic contractions, lack of dilatability of the cervix, the effect of drugs on the uterine musculature in the pregnant and nonpregnant state and many more problems, because most likely the action of the monkey's uterus is similar to that of woman.)

The studies of Calkins, Litzenberg and Plass⁹⁷ on the length of labor lead them to believe that a more accurate observation of the resistance of the cervix and the pelvic floor as well as a more accurate determination of the effectiveness of the labor pains, will be necessary in order to analyze the causes for the extreme variations in the length of labor so commonly encountered. The authors make suggestions concerning the recording of information about the cervix before and during labor and of the uterine contractions. (There is no doubt at all that not enough attention is paid to the study of the cervix during the last few weeks of pregnancy and during labor, and to uterine contractions during labor unless the latter is unusually prolonged. These studies are very important because in this country at least there is much more dystocia from the soft parts, [the cervix and the perineum] than from bony pelvic contractions. The length, shape, and consistency of the cervix and the frequency, duration, and especially the intensity of the uterine contractions are the most important factors in the determination of the duration of labor.)

Greenhill⁹⁸ reports in detail the type of intrapartum care given the patients at the Chicago Lying-in Hospital and cites the results. Among 23,136 labor cases there were 57 maternal deaths (24.6 per 10,000) and

the important causes of death were pneumonia 14, toxemia 10, heart disease 9, abruptio placentae 6, embolism 5, peritonitis 4, septicemia 3, and rupture of the uterus 3. Toombs⁹⁹ discusses the management of the first and second stages of labor. (A large proportion of patients are sadly neglected during labor. Because women in the first stage are treated conservatively and properly so, many of them are actually neglected until the child is ready to be born. Patients in labor need much more than a narcotic. It is important that the patient take fluids and nourishment, that her bladder and bowels be properly emptied, that she secure enough rest, that her courage be maintained especially if labor is prolonged, that examinations be made from time to time to determine the progress of labor and that the surroundings be kept as clean as possible. Special precautions are, of course, necessary in the second and third stages of labor and for at least an hour after the placenta has been delivered. There is no doubt whatever that proper care during labor will save the lives of numberless women. Good prenatal care has prevented thousands of deaths during the last few decades and in spite of this fact, just as many women die today from childbirth as died thirty years ago. This seeming paradox is due to the fact that what we save during pregnancy, we lose during labor by lack of care and by the tremendous increase in the incidence of operative deliveries. The number of forceps deliveries, versions and extractions and cesarean sections should be curtailed precipitously, especially by those who are not skilled obstetricians.)

Quigley¹⁰⁰ believes that the dangers associated with pregnancy and labor in women over thirty years of age have been greatly exaggerated. Losell¹⁰¹ compared a series of primiparas forty or more years of age with series of primiparas between twenty and twenty-five years and between thirty and thirty-five years. He found that as the age increased, there was an increased incidence of forceps deliveries and an increase in fetal mortality. Nixon¹⁰² studied a group of primiparas between forty and forty-five years old and found a maternal death rate of 4 per cent, a fetal mortality of 17 per cent, a higher incidence of toxemia and longer labors than among young women. Vermelin and Vaisbuch¹⁰³ collected from the literature 20 cases where women over fifty years of age became pregnant. There were no cases of toxemia but 5 of the 20 women had an hydatidiform mole. (Most likely the risk of labor in elderly primiparas has been overemphasized. We must distinguish between the elderly woman who has been married many years before she could conceive and the woman who married late in life and became pregnant immediately afterward. The latter will in most cases have a labor similar to that in young women, but the former may have trouble. In general it may be said that toxemias occur more frequently in older women and relatively more of them have hydatidiform moles. It is entirely too radical to perform a cesarean section simply because a patient is over forty years of age. However, since greater value should be placed upon the life of a baby in such a woman we should be willing to perform this operation when there are present such additional factors as breech presentation, moderate pelvic contraction, toxemia, or other complications.)

Series of cases in which labor was induced by means of castor oil, quinine and pituitary extract are reported by Mathieu and Siehel,¹⁰⁴ Fournier,¹⁰⁵ and Dodds.¹⁰⁶ The first authors report success in 96.6 per cent of 320 cases whereas the last one obtained satisfactory results in

only 54 per cent of his 338 cases. Vignes^{106a} praises formalin as an oxytocic. The studies of Schübel¹⁰⁷ showed that weak concentrations of quinine stimulate the isolated rabbit uterus whereas strong concentrations paralyze it. Hence in obstetrics only small doses of quinine should be used. Sztchlo¹⁰⁸ believes that premature rupture of the bag of waters is dangerous for both mother and child whereas Guttmacher and Douglas¹⁰⁹ recommend artificial rupture of the membranes as a safe and efficient method of inducing labor. (The question of induction of labor requires clarification. There are, of course, numerous instances when induction is necessary but in a large number of cases, labor is induced for the convenience of the physician or the patient. If a reliable and safe procedure can be made available, no great harm will result, unless vaginal manipulation is included in the procedure. In this case there is always the risk of infection. There are a few instances where quinine was most likely responsible for fetal death but the number is very small. The reviewer has always maintained that there is no necessity to give large doses of quinine to induce labor and the experiments of Schübel are gratifying because they tend to support this contention. Pituitary extract alone for the induction of labor is not often successful. The most certain way of inducing labor is rupture of the bag of waters but this always carries with it the risk of infection and of prolapse of the cord. However, if an experienced obstetrician would carry out this procedure in cases where the fetal head is engaged, under strict aseptic precautions, he will obtain excellent results. This statement is contrary to the belief we formerly held that rupture of the membranes was serious for the mother because of danger of infection and injury to the cervix, and it endangered the baby's brain because of direct pressure of the latter against the cervix. I have resorted to rupture of the membranes in many primiparas and multiparas and thus far my results have been excellent.)

Thymophysin is again the subject of many papers. This drug is highly praised by Lork¹¹⁰ and Temesvary¹¹¹ but it is condemned by Nelson,¹¹² Bauer,¹¹³ Fecht¹¹⁴ and Halley and Whiteley.¹¹⁵ (I¹¹⁶ recently made a comparison of thymophysin and 25 per cent U. S. P. pituitary extract in a series of cases and a few of my conclusions are as follows: Weak pituitary solution and thymophysin are seldom effective for the induction of labor. They should not be used in the second stage except on rare occasions. Both drugs when administered during the first stage shorten labor in some cases. If these substances are used during the first stage they should be given only for a definite indication such as uterine atony or some urgent reason for shortening labor and only small doses should be given, namely, 3 minims or less. The 25 per cent pituitary extract and thymophysin give almost the same clinical results. Occasionally both preparations even in small doses may do harm. Both have a tendency to increase the blood pressure, and to result in incomplete relaxation of the uterus between pains and both may produce irregularities in the fetal heart rate.)

Analgesia and Anesthesia.—De Lee¹¹⁷ takes up in detail the indispensable use of narcotics in obstetrics. Whitaker¹¹⁸ praises the rectal administration of avertin for the relief of labor pains whereas Lewis and Hamilton¹¹⁹ favor the intravenous and intramuscular use of sodium amytal. Hamblen and Hamblin¹²⁰ believe the oral administration of sodium amytal is just as satisfactory as the intravenous route. Stander¹²¹ recommends avertin as an anesthetic when general inhalation anesthesia

is contraindicated. Bode¹²² and also Brown, Moloy and Laird¹²³ are of the belief that pernocton is a harmless and efficient analgesic in labor. In a symposium on the relief of pain during labor held before the Massachusetts State Medical Society, papers were presented by McCann,¹²⁴ O'Connor,¹²⁵ Parkhurst,¹²⁶ and Shay.¹²⁷ Pierce¹²⁸ is enthusiastic about the use of direct infiltration anesthesia not only for cesarean section but also for episiotomies and low forceps operations. Aburel¹²⁹ and De Peretti¹³⁰ also favor regional anesthesia but Klaus¹³¹ recommends lumbar anesthesia for cesarean section. Cosgrove¹³² maintains that nupercaine is less desirable than novocaine for spinal anesthesia in obstetrics. (Analgesia and anesthesia are important subjects in obstetrics. In spite of propaganda every few years in both medical literature and lay magazines in favor of new preparations and methods of relieving the pains of labor, morphine and pantopon remain the two safest and most reliable drugs. Avertin has a narrow margin of safety, pernocton produces excitation and sodium amytal is still on trial. As for anesthesia it is gratifying to see the increased popularity of local anesthesia especially by direct infiltration for episiotomy, low forceps, and cesarean section. All inhalation anesthetics entail some risk, especially in the presence of toxemia; and these dangers may be avoided or diminished by means of local anesthesia. Direct infiltration is safer and just as effective as spinal anesthesia, hence, it is preferable. The technic of its use is extremely simple and should be familiar to all who operate.)

Operative Obstetrics.—Rucker^{133, 134} again emphasizes the value of adrenalin in the treatment of contraction ring of the uterus. (This is a very valuable suggestion.)

The records of large groups of breech presentations are analyzed by Westman,¹³⁵ Gibberd,¹³⁶ Dearnley,¹³⁷ Bourne,¹³⁸ Dunbar¹³⁹ and Tausig.¹⁴⁰ The last named author emphasizes a number of very important rules which should be observed. (A breech delivery is the best test of an obstetrician's ability, because it requires an exact knowledge of the mechanism of labor, judgment as to the time of interference, a great deal of patience, skill in the extraction and the use of forceps on an after-coming head, gentleness, and a cool head. Since breech deliveries have a rather high fetal mortality among multiparas as well as among primiparas it is advisable to perform an external version during the last few weeks of pregnancy whenever this can be accomplished without undue force and manipulation. The Trendelenburg position may aid in this maneuver.)

Dennen¹⁴¹ and Zweifel¹⁴² report new types of forceps and Harper^{142a} describes the application of forceps. (Most obstetricians become adept with one type of forceps, and they can accomplish with this one instrument nearly everything which is claimed for new instruments devised for special purposes.)

The treatment of occipitoposterior position is discussed by Dodek,¹⁴³ Bill,¹⁴⁴ and Taylor.¹⁴⁵ Bill delivers most patients who have this complication by means of internal podalic version and breech extraction or by a modified Scanzoni forceps delivery. (In cases of persistent occipitoposterior the reviewer resorts to manual rotation of the head rather than rotation with the forceps because he believes it is less likely to produce harm to both mother and child. In cases where the head is high it is far safer to perform version and extraction than to attempt a high forceps operation with its danger to the mother and serious

consequences for the child. However, these operations should be performed only by experienced obstetricians and not by neophytes.)

In an excellent, extensive discussion, Plass¹⁴⁶ shows the relationship of forceps delivery and cesarean section to maternal and infant mortality and morbidity. (In this article Plass clearly demonstrates the harm which has resulted from the greatly increased incidence of operative deliveries. He points out the causes and remedies of this deplorable state of affairs and for this reason every physician should be familiar with the contents of Plass' paper. It is most regrettable that general practitioners, with limited obstetric experience, who see the excellent results obtained by well-trained obstetricians in specially equipped maternity hospitals, try to do the same things in general hospitals, some of which are none too clean, and with disastrous results.)

As usual a large number of articles have appeared on cesarean section. The general indications for this operation are reviewed by Winter¹⁴⁷ and analyses of large groups of cases are reported by many authors. Tollas¹⁴⁸ reports 252 cases with a death rate of 6 per cent. Phaneuf,¹⁴⁹ 418 cases with a mortality of 5 per cent. Johnston and Smith,¹⁵⁰ 258 cases with 10.5 per cent fatalities, and Greenhill,¹⁵¹ 140 personal cases with no deaths.

The indications for, and the results of Porro operations are discussed by Phaneuf.¹⁵² The technic of cesarean section under local infiltration anesthesia is described by Williamson,¹⁵³ and Kreis¹⁵⁴ analyzes the deaths following low cervical cesarean sections. Hornung¹⁵⁵ found that of 111 women who were delivered by the cervical cesarean section and subsequently became pregnant 57 were delivered vaginally. Holterman¹⁵⁶ prefers the extraperitoneal to the transperitoneal cervical operation. Campbell and Miller¹⁵⁷ review the subject of post-mortem cesarean section. (The old controversy continues concerning the relative merits of the classic, the transperitoneal cervical and the extraperitoneal cervical operations. Likewise there is a division of opinion as to whether the transverse is better than the longitudinal incision in performing the low operation. The consensus of opinion and the results in large series indicate that the cervical operation is superior to the classic one, and most individuals prefer the transperitoneal to the extraperitoneal operation. Likewise the longitudinal incision is the popular one. Porro operations have a definite though limited field and represent the only type of abdominal operation to be performed in frankly infected cases. Local anesthesia greatly diminishes the risk of cesarean section. In spite of this and in spite of the excellent results reported by individual operators or clinics, there should be a marked decrease in the number of these operations, especially by general surgeons and practitioners, because in their hands the maternal death rate is about ten per cent.)

Uterine Hemorrhage.—Calkins, Litzenberg, and Plass¹⁵⁸ analyzed 5,600 cases with reference to the amount of blood lost in the third stage of labor and they recommend a definite technic for the management of the placental stage. Smith¹⁵⁹ outlines the Dickinson-Pomeroy method of third stage technic. (These authors properly recommend conservatism with the aid of pituitary extract and ergot. As soon as there is evidence of separation of the placenta, the latter should be expressed by squeezing the uterus, but first we should be certain the uterus is

contracted and in the midline. It is dangerous to massage the uterus before the placenta has separated. Since the third stage of labor is just as important as the first or second and often more so, the physician should not be impatient and attempt to cut it short.) Placintianu¹⁶⁰ discusses the treatment of late postpartum hemorrhages and a number of papers deal with placenta previa. Rucker's¹⁶¹ main reliance in the treatment of placenta previa is the number 5 Voorhees bag, usually placed extraovularly and followed by version and extraction. He had five maternal deaths in a series of 141 cases (3.5 per cent). Thiemke¹⁶² also treated his cases conservatively and among his 228 cases the mortality was 6.1 per cent. In Peckham's¹⁶³ series of 146 cases which were treated essentially by colpeurynters, the death rate was 8.6 per cent. Bill¹⁶⁴ on the other hand, is strongly in favor of cesarean section with the aid of blood transfusion. He had only 2 maternal deaths among 104 cases. Others who favor cesarean section for placenta previa are Palliez¹⁶⁵ and Siegel.¹⁶⁶ Rotthaus¹⁶⁷ discusses the relative merits of cervical and corporeal cesarean section for placenta previa, whereas Essen-Möller¹⁶⁸ recommends vaginal cesarean section. (The reviewer is of the opinion that most women with central or partial placenta previa should be delivered by cesarean section, provided the patient is in a clean hospital and the physician has had sufficient experience with this operation. The safest type of cesarean is the cervical one. There need be no more fear of encountering the placenta in this type of operation than in the classic one. If the patient is potentially or actually infected and especially if she has a number of living children, a Porro operation should be performed. A transfusion should be given to patients who have lost much blood and local anesthesia should be used to prevent further diminution of the patient's resistance. There is no necessity to make a vaginal or even a rectal examination in a patient's home in order to make a diagnosis. Either of these types of examination may lead to serious hemorrhage. Every pregnant woman who has a hemorrhage should be sent to a hospital preferably without an internal examination or vaginal pack. If a woman must be delivered at home the best procedure is rupture of the membranes, firm packing of the vagina with wet cotton pledgets, and a Braxton-Hicks version. Likewise, in a hospital, delivery through the vagina is the method of choice in cases of marginal placenta previa and in a few cases of central and partial previas. Here a colpeurynter is more advisable than a Braxton-Hicks version. If a patient is to be delivered from below, the physician should remain with the patient constantly until the baby and placenta are delivered.)

Davis and McGee¹⁶⁹ have written an elaborate paper on abruptio placentae. They report 164 cases from the Chicago Lying-In Hospital with a maternal mortality of 7.3 per cent and a fetal death rate of 59.7 per cent. In the grave cases chief reliance was placed upon cesarean section. Kornfeld¹⁷⁰ favors conservative therapy in cases of abruptio placentae. In 50 cases at the Jewish Hospital (Brooklyn) there were no maternal deaths. Polak¹⁷¹ also believes in conservatism and he gives in detail the etiology, symptomatology, prognosis, and treatment of this condition. (Abruptio placentae may be very mild and on the other hand it may be rapidly fatal. The mild cases can certainly be treated conservatively. Since they generally occur during labor, the latter can usually be terminated by a forceps delivery or

version and extraction. In serious cases morphine and a blood transfusion should be given, the bag of waters ruptured, the vagina firmly packed with wet cotton pledgets, and a few small doses of pituitary extract given. The pulse rate, blood pressure, hemoglobin, and red blood cell count should be controlled at frequent intervals. If labor seems to progress and the patient's general condition does not become worse, delivery from below should be awaited. If, however, bleeding continues and the patient's condition becomes aggravated, a cesarean section should be performed under local anesthesia without delay. If the uterus presents the picture of uteroplacental apoplexy, it should be removed.)

PUERPERIUM

General.—Galloway,¹⁷² Lash,¹⁷³ Hanna¹⁷⁴ and Greenhill¹⁷⁵ all discuss postpartum care. (There are numerous prenatal clinics throughout the country and the results of their work amply justify their continued maintenance. On the other hand, there are comparatively few postpartum clinics in spite of the fact that this care after pregnancy is most essential. For most physicians, postpartum care consists of a small amount of attention for ten or twelve days after delivery and then a so-called final examination at the end of six or eight weeks. Furthermore, this examination is usually a cursory one. All women should be examined at least three times during the first twelve months after a baby is born. The cervix should always be inspected as well as palpated. Pathologic conditions should be corrected. Patients who have had toxemia, pyelitis or other complications during pregnancy or the puerperium, require special care after delivery.)

One of the greatest contributions in recent years is J. W. Williams'^{176, 177} description of the disappearance of the placental site during the puerperium. Williams' study showed unequivocally that the placental site is not absorbed as was formerly believed, but is undermined by proliferation of endometrial tissue and eventually exfoliated. This process usually requires six or seven weeks. (Every physician should carefully read this valuable article which was the last paper written by one of the greatest obstetricians in the world.)

Sepsis.—The experimental and clinical results obtained by Green, Pindar, Davis, and Mellanby¹⁷⁸ indicate that an adequate supply of vitamin A must be given to pregnant women. These authors found that 1.1 per cent of their vitamin treated cases as compared with 4.7 per cent of their control cases developed morbidity. Logan¹⁷⁹ found that a deviation from the ideal type of vaginal flora during pregnancy seemed to have little or no effect upon the production of puerperal sepsis. Brindeau and Vourkievitch¹⁸⁰ found a relationship between streptococci in the mouth of pregnant women and fever during the puerperium. Hence, they suggest that the throats of pregnant women be disinfected near term and those in attendance wear masks. (I have repeatedly stressed the importance of the use of masks in delivery rooms. Not only should the physician who is to do the delivery wear a mask but also the nurses, the assistants, the anesthetist and all onlookers. The mask should cover not only the mouth but also the nose. The patient also should wear a mask in the delivery room until she is to be anesthetized. These precautions are doubly important during the seasons of the year when grippe is prevalent.)

Welton, Glass and Mazzola¹⁸¹ point out the flaws in our present method of determining morbidity and they recommend that we list as morbid every patient who gives evidence of any definite or prolonged pathologic condition with or without fever, directly resulting from childbirth. (The authors are correct in maintaining that our present standards of morbidity are fallacious. We need uniform criteria for determining morbidity especially for the purpose of comparison.) Vignes¹⁸² discusses the acute infections of the mammary gland during lactation and Granzow¹⁸³ recommends roentgen ray treatment for this condition. (To be effective the x-rays must be used before suppuration has set in. If pus is present one or more incisions must be made.)

Harmon¹⁸⁴ shows that during the years 1922 to 1927, with the possible exception of the rural white population in this country, the death rates from puerperal septicemia have not declined among the groups studied (urban white, rural white, urban colored, and rural colored), and furthermore, the rates for each division have remained remarkably constant. (Puerperal septicemia is responsible for about 40 per cent of all maternal deaths and in spite of improvements in obstetrics its incidence has remained practically constant not only in the United States but in foreign countries as well. The chief reason for this is the increased incidence of operative deliveries and a marked augmentation in the number of criminal abortions.)

For the treatment of puerperal sepsis, Litwak¹⁸⁵ recommends transfusion of the patient's own blood, Kriel¹⁸⁶ favors antistreptococcus serum, Finger¹⁸⁷ suggests the administration of cholesterin, Fauvet¹⁸⁸ uses intravenous continuous drip transfusion of glucose solutions and Sorrentino's¹⁸⁹ therapy consists of a veritable bombardment of manipulation. He begins by giving antistreptococcus serum, then injections of the patient's own milk or cow's milk, urotropin intravenously, intramuscular injection of the patient's own blood, hypodermies of quinine and finally fixation abscesses produced by the injection of turpentine. (We ought to pity Sorrentino's patients. As yet we have no specific for puerperal sepsis. With the exception of blood transfusions, all intravenous therapy including alcohol, electrargol, collargol, rivanol, anelm dyes, salvarsan, meurochrome, etc., has failed to give even encouraging results. Likewise antistreptococcus serum has failed in most instances. The only thing we can do is build up the patient's resistance by bedrest, abundant fluids, glucose, nourishing food, sunlight, fresh air, and small blood transfusions.)

THE NEWBORN

Physiology.—Notwithstanding reports in the literature, Toombs¹⁹⁰ is of the opinion that there is no relationship between the mother's gain in weight during pregnancy and the infant's birth weight. Schmidt¹⁹¹ reports the case of a baby which was delivered spontaneously 274 days after the beginning of its mother's last menses and which weighed 5,500 gm. and measured 59 cm. in length. The author points out that this child probably weighed 3,600 gm. six weeks before term and almost 3,000 gm. eight weeks before delivery. Hence, this is indirect proof that a child born 230 days after the mother's last menses may have all the signs of maturity. Eparvier¹⁹² maintains that the centers of ossification of a newborn cannot be used as criteria of the intrauterine age of a fetus or of its maturity. (Schmidt's case is im-

portant in medicolegal cases. The reviewer agrees with Toombs. Women should not be permitted to gain too much weight for their own sake and not because of the erroneous belief that they will give birth to large babies.)

Complications.—Lyon and Bemis¹⁹³ analyze 117 neonatal deaths which occurred among 6,000 deliveries (2 per cent). There were 58 premature babies in this series and only 55 of the 117 babies were delivered normally. Cerebral hemorrhage was found in 25 out of 67 autopsies (37.7 per cent). Tyson and Crawford¹⁹⁴ found that 32.1 per cent of the babies in their series which came to autopsy had cerebral hemorrhage. In the series of 11,236 deliveries studied by Pigeaud and Brochier,¹⁹⁵ the fetal death rate was 7.8 per cent. Obstetric trauma caused 29.1 per cent of the deaths and syphilis was responsible for 22.3 per cent more. (In this country syphilis causes relatively few fetal deaths among white women. Prematurity, cerebral hemorrhage, toxemia and congenital malformations are much more frequent causes. A large proportion of fetal deaths can be prevented by good prenatal care, proper supervision during labor, conservative deliveries and special preparations for premature babies.)

Lazar¹⁹⁶ reports 80 cases of ophthalmia neonatorum of which 36 were of gonorrheal origin. (The instillation of silver nitrate or other silver preparation is required by law, and we take it for granted that every child is given this prophylactic treatment. Yet Lazar reports 36 cases of gonorrheal ophthalmia. This matter is serious when we realize that as late as 1922 Waldeck reported that 25 per cent of the blindness in the United States was due to ophthalmia neonatorum.)

A few epidemics of impetigo contagiosa neonatorum are reported by Swendson and Lee¹⁹⁷ and their treatment is as follows: Each vesicle is opened with an applicator dipped in alcohol and the base is swabbed with 5 per cent solution of silver nitrate. Taylor's dusting powder is applied freely to the whole body. (In addition to this the whole body should be exposed to the air and sunlight or to a therapeutic lamp. Strict isolation of each case, especially the first one, is imperative.)

In a symposium on resuscitation of the newborn, papers were presented by Coryllos,¹⁹⁸ Flagg,¹⁹⁹ Henderson,²⁰⁰ Crothers,²⁰¹ Kosmak,²⁰² and Murphy, Wilson, and Bowman.²⁰³ (This symposium is well worth reading because in it are expressed the viewpoints of physiologists, surgeons, anesthetists, neurologists, and obstetricians. As might be expected, there is no unity of opinion. The important things in resuscitation of the newborn are warmth, clearing the respiratory passages of mucus and other material and insufflation of air or oxygen. Most babies can be resuscitated by means of a tracheal catheter. For those not familiar with this simple life-saving device, the Drinker or the Kreiselman-Kane-Swope apparatus will be of considerable help. Foreible measures are to be condemned.)

THE PLACENTA

Various methods of determining the intactness of placentas were studied by Luh,²⁰⁴ and he came to the conclusion that inspection was the most reliable. Eastman²⁰⁵ found that following antenatal arsphenamine therapy, arsenic is retained in the human placenta for as long as fifteen days after the last treatment. The storage of arsenic and especially its greater concentration in the fetal part may be an im-

portant factor in the beneficial action upon the fetus resulting from arsphenamine treatment. (There is no doubt about the effectiveness of intensive antisypilitic treatment during pregnancy in decreasing the fetal mortality due to syphilis.)

Montgomery²⁰⁶ presents a biologic and histologic study of infarction of the placenta. He prefers the term "necrosis" to "infarction" because the process begins with small areas of tissue death rather than with obstruction of circulation. (Montgomery is correct in preferring the term necrosis, first because the lesion has its origin in degeneration of the syncytium of the chorionic villi and secondly because the term infarct suggests an embolus which of course is not to be found.)

MISCELLANEOUS

In February, 1931, the White House Conference on Child Health and Protection was held in Washington, D. C. Adair²⁰⁷ made his address as chairman of the Committee on Prenatal and Maternal Care, Findley²⁰⁸ spoke on "The Undergraduate Teaching of Obstetrics," Holmes²⁰⁹ presented his report on "Graduate Education of Physicians in Obstetrics," Kosmak²¹⁰ spoke on "Obstetric Training of Nurses and Attendants," McCord's²¹¹ subject was "The Education of Midwives," Polak²¹² discussed "Maternal and Early Infant Care" (the last paper of one of our greatest teachers of obstetrics), Ehrenfest²¹³ spoke on the "Factors and Causes of Fetal, Newly Born, and Maternal Morbidity and Mortality," and Arey²¹⁴ took up the subject of "The Basic Sciences and Their Relation to Maternal and Fetal Problems." (These papers, presented by the chairmen of the various committees represent the results of studies made by the leading authorities in this country. Not only should the above reports be read but also, if obtainable, a copy of the Supplement to The United States Daily, Section II, Vol. VI, No. 29, April 6, 1931. This supplement contains valuable information.)

Another paper²¹⁵ devoted to improvement in the teaching of obstetrics is that which contains the recommendations made by the Committee on Maternal Welfare of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons. Findley²¹⁶ shows that as compared with surgery, the teaching of clinical obstetrics is woefully lacking in the major portion of our medical schools. (This is very unfortunate because a young practitioner is likely to develop a far greater obstetric practice than a surgical one. He takes many more chances with a patient in labor before calling a consultant than he does with a patient who requires a major surgical operation.)

A number of papers are devoted to maternal mortality, among them being those by McCusker²¹⁷ for the state of Oregon, Burkhard²¹⁸ for Colorado, Frank and Kushner²¹⁹ for Bronx Hospital, Starr²²⁰ for the Louisville City Hospital, Knox²²¹ for Maryland and Bell²²² for England and Wales. (All authors are agreed that the maternal mortality in the United States is far too high, but we should not keep repeating the utterly fallacious statement that our mortality rate is higher than it is in nearly every civilized country in the world. Regardless of this we can and should considerably decrease our obstetric deaths by improving the education of medical students, increasing the facilities for postgraduate instruction in obstetrics, adding more maternity hospitals and securing better quarters for obstetric patients in general hospitals, educating physicians to develop an honest obstetric con-

science, secure proper prenatal care for more women, considerably decrease the number of operative deliveries and educate the laity to the dignity and importance of obstetrics as a specialty. Undoubtedly the recently created Board of Obstetrics and Gynecology will do a great deal toward eliminating unnecessary maternal and fetal deaths.)

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185 NORTH WABASH AVENUE.

American Board of Obstetrics and Gynecology

The following additional names of men limiting their practice to Obstetrics and/or Gynecology have been approved for certification by the American Board of Obstetrics and Gynecology.

Arizona, Tucson: H. H. Ring.	ter, New York City; Benjamin Rab-
Colorado, Denver: Cuthbert Powell.	binner, New York City; R. N. Ritchie,
District of Columbia, Washington: J. J.	Rochester.
Mundell, R. Y. Sullivan, E. W. Titus,	North Carolina, Kinston: T. L. Lee.
Prentiss Willson.	Ohio: W. D. Fullerton, Cleveland; An-
Illinois, Chicago: Harry Sered.	drews Rogers, Columbus.
Iowa, Cedar Rapids: W. E. Brown.	Oklahoma, Tulsa: P. N. Charbonnet.
Kansas, Wichita: R. A. West.	Pennsylvania: Leon Clemmer, Philadel-
Louisiana, New Orleans: W. E. Levy.	phia; E. B. Craig, Philadelphia; J. E.
Maryland, Baltimore: L. H. Douglas.	James, Jr., Philadelphia; David Katz,
Massachusetts, Boston: E. P. Ruggles,	Pittsburgh.
E. W. Smith.	Tennessee, Memphis: P. C. Schreier.
Minnesota, St. Paul: A. G. Schulze.	Texas, San Antonio: W. W. Maxwell,
Missouri, Springfield: J. D. James.	B. H. Passmore.
New York: H. E. Ayres, New York	Vermont, Burlington: O. N. Eastman.
City; Adolph Bonner, Brooklyn; C. R.	Virginia, Richmond: B. H. Gray.
Hyde, Brooklyn; Theodore Neustaed-	Syria, Beirut: H. G. Dorman.

At the recent meeting and examination of the American Board of Obstetrics and Gynecology held in New Orleans, on May 10, 1932, fifteen applicants were accepted for certification. Three failed to receive the required grades.

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Books Received

GROWTH IN THE FETAL PERIOD. By Richard E. Scammon, Professor of Anatomy, University of Minnesota, and Leroy A. Calkins, Professor of Obstetrics and Gynecology, University of Kansas. The University of Minnesota Press.

CLINICAL STUDY OF THE ABDOMINAL CAVITY AND PERITONEUM. By Dr. Edward Meakin Livingston, Associate Visiting Surgeon, Bellevue Hospital, New York, 1932.

EUGENESIA Y MATRIMONIO. Dr. Francisco Haro Garcia. Editor: Javier Morata, Madrid, 1932.

DIE KONSERVATIVE BEHANDLUNG ENTZUENDLICHER GENITALER-KRANKUNGEN DER FRAU. Von Dozent Dr. Gustav Doederlein, Universitaets-Frauenklinik der Charite in Berlin. Mit 7 Abbildungen. Verlag von Georg Thieme, Leipzig, 1932.

TEXTBOOK OF GYNAECOLOGY. By Sidney Forsdike, Surgeon to the Hospital for Women, Soho Square, etc. London, William Heinemann, 1932.

GYNAEKOLOGISCHE OPERATIONSLEHRE. Von Hofrat Professor Dr. Josef Halban in Wien. Urban und Schwarzenberg, Wien, 1932.

SURGICAL PATHOLOGY OF THE FEMALE GENERATIVE ORGANS. By Dr. Arthur E. Hertzler, Surgeon to the Agnes Hertzler Memorial Hospital, Halstead, Kansas, and Professor of Surgery, University of Kansas. 258 illustrations, J. B. Lippincott Company, Philadelphia, 1932.

FERTILITY AND STERILITY IN MARRIAGE. Their voluntary promotion and limitation. By Dr. H. van de Velde, formerly Director of Gynecologic Clinic in Harlem, Holland. New York, Covici, Friede, Medical Books, 1932.

CONTROL OF CONCEPTION. An illustrated medical manual. By Dr. Robert Latou Dickinson and Louise Stevens Bryant, The Williams & Wilkins Company, Baltimore, 1931.

THE PRACTICE OF CONTRACEPTION. An international symposium and survey. Edited by Margaret Sanger and Dr. Hannah M. Stone. The Williams and Wilkins Company, Baltimore, 1931.

HUMAN STERILIZATION. By J. H. Landman, Ph.D., J.D., J.S.D. College of the City of New York. The Macmillan Co., New York, 1932.

PRACTICAL MEDICINE SERIES. Obstetrics edited by Joseph B. DeLee. Gynecology edited by J. P. Greenhill. Series 1931. Year Book Publishers, Inc., Chicago, 1932.

GEBURTSHELPER UND ROENTGENBILD. Von Univ. Professor Dr. Wilhelm Liepmann und Dr. Gerhard Danelius. Mit 160 Abbildungen. Urban und Schwarzenberg, Berlin und Wien, 1932.

REGULATION DES SAEURE-BASEN HAUSHALTS IN SCHWANGERSCHAFT etc. Von Privatdozent Dr. Karl Julius Anselmino. Mit 11 Abbildungen. S. Karger, Berlin, 1932.

LA TUBERCULOSE GENITALE DE LA FEMME. Par Professeur Constantin Daniel, Faculté de Medecine de Bucarest. G. Doin & Cie. Paris, 1932.

TRATADO DE OBSTETRICIA. Por Dr. D. Sebastian Recasens Girol, con varios capitulos originales del Dr. D. Luis Recasens Serrano. Sexta Edicion, con 430 grabados en el texto y 20 lamnias. Salvat Editores, S. A. Barcelona, 1932.

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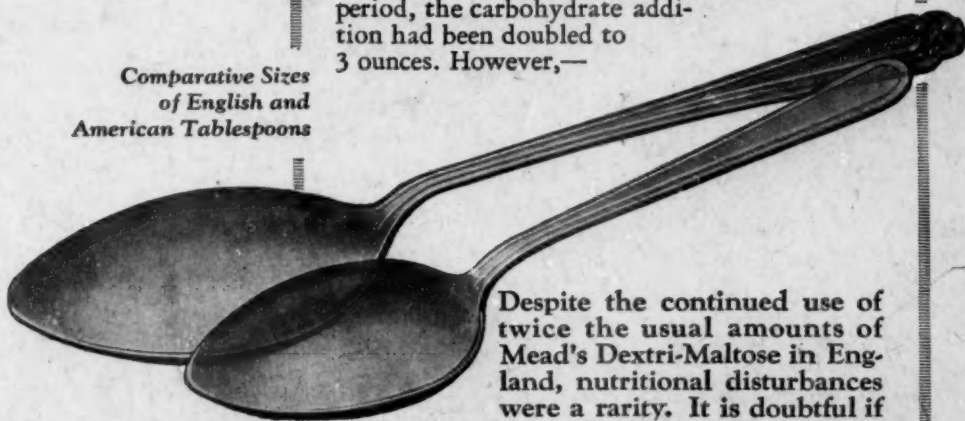
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M.D., Waco, Texas.

J.A.M.A.,
Dec. 19, 1931,
p. 1914

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